



Module 3
CDC/UNMC
Select Agents and Toxins
Training



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04/2006


Select Agents and Toxins
Module 3

- Information about this training module
 - For a **comment or to ask a question**, you will find a link on the main page of the course.
 - To enhance the size of this PowerPoint presentation, click on the “screen icon” at the bottom right of this page
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Who must receive this training?

- Individuals who possess, handle, and/or transfer select agents or toxins.
- Training must be done annually.
- Record verification of training.


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Select Agents and Toxins
Module 3 Outline

- Federal Rules
- Registration Requirements
- Working with Select Agents


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Definitions

- Select Agents and Toxins
 - biological agents and toxins that have been determined to have the potential to pose a severe threat to human health, to animal health, to plant health, or to animal and plant products.
- Overlap Select Agents and Toxins
 - agents included on both the Health and Human Services list and the US Department of Agriculture list.


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What federal rules regulate the possession, use, receipt, or transfer of these agents?

- Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism Act of 2001 (USA PATRIOT Act)
 - regulates possession
 - defines individuals who are “restricted” from having access to or possessing any amount of these agents.

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Federal Rules (continued)

- 42 CFR Part 73, Possession, Use, and Transfer of Select Agents and Toxins, Final Rule, March 18, 2005
 - Supercedes the regulations in 42 CFR 72.6 (effective April 15, 1997) to establish requirements for labs to receive and transmit select agents.
 - Gives the HHS and USDA the authority and responsibility for regulating activities regarding these agents to protect the public health and safety.

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List of Select Agents and Toxins

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Multiple lists

- HHS list
 - only regulated by this organization
- USDA list
 - only regulated by this organization
- HHS/USDA list
 - regulated by both organizations
 - UNMC is registered with HHS through the CDC to work with select agents.

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HHS List (not inclusive)

- Viruses
 - Crimean-Congo haemorrhagic fever virus
 - Ebola virus
 - *Cercopithecine herpesvirus 1* (Herpes B virus)
 - Lassa fever virus
 - Marburg virus
 - Monkeypox virus
 - South American Haemorrhagic fever viruses
 - (Junin, Machupo, Sabia, Flexal, Guanarito)
 - Tick-born encephalitis complex (flavi) viruses
 - (Central European tick-born encephalitis, Far Eastern tick-borne encephalitis [Russian spring and summer encephalitis, Kyasanur forest disease, Omsk hemorrhagic fever])
 - Variola major virus (Smallpox virus)
 - Variola minor virus (Alastrim)



HHS List (not inclusive)

- Bacteria
 - *Rickettsia prowazekii*
 - *Rickettsia rickettsii*
 - *Yersinia pestis*

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HHS List (not inclusive)

- Toxins
 - Abrin
 - Conotoxins
 - Diacetoxyscirpenol
 - Ricin
 - Saxitoxin
 - Tetrodotoxin
 - Shiga-like ribosome inactivating proteins

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HHS List

- Genetic elements
 - Viral nucleic acids that can encode infectious and/or replication competent forms of any select agent virus.
 - Nucleic acids that encode for the functional form of any regulated toxins.
 - Viruses, bacteria, fungi, and toxins on the HHS list that have been genetically modified.

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HHS / USDA Overlap List (not inclusive)

- Viruses
 - Eastern Equine Encephalitis virus
 - Nipah and Hendra complex viruses
 - Rift Valley fever virus
 - Venezuelan equine encephalitis virus

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HHS / USDA Overlap List (not inclusive)

- Bacteria
 - *Bacillus anthracis*
 - *Clostridium botulinum*, neurotoxin producer
 - *Brucella abortus*
 - *Brucella melitensis*
 - *Brucella suis*
 - *Burkholderia mallei*
 - *Burkholderia pseudomallei*
 - *Coxiella burnetii*
 - *Francisella tularensis*



HHS / USDA Overlap List (not inclusive)

- Fungus
 - *Coccidioides immitis*
- Toxins
 - Botulism neurotoxin
 - Shigatoxin
 - Staphylococcal enterotoxins
 - T-2 toxin
 - Epsilon toxin from *Clostridium perfringens*

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What forms of select agents are regulated?

- Live biological agents and toxins
- Nucleic acids that encode infectious and/or replication competent forms of listed viruses.
- Nucleic acids that encode for the functional form of the listed toxins.
- Genetically modified select agents and toxins.

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How are toxins regulated?

- Based on potency (LD50 value) and quantity.
- Regulation 49CFR Part 73 gives a listing of the requirements.

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*What forms of select agents are **not** regulated?*

- Agents or toxins present in their natural occurring environment.
- Non-viable select agents or nonfunctional toxins.
- Certain vaccine strains.
- Regulated toxins which are below listed quantities and have a potency below listed standards.

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Registration Requirements



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Who is affected by the select agent regulations?

- Institutions that possess select agents or toxins
 - must register with the HHS and/or USDA.
 - the Institution is responsible to identify those individuals who have access to and/or possess select agents and toxins.
- Individual investigators who work with or possess these agents
 - must register through the Institution.

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*Who is **exempt** from the regulations?*

- Institutions that do not possess select agents or toxins.
- Institutions with diagnostic or clinical labs which perform diagnostic, verification, or proficiency testing only
 - any identified select agent or toxin must be reported to HHS or USDA and subsequently, the agent must be transferred to a registered facility or destroyed.

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Why do I need to register in order to possess or use select agents or toxins?

- These agents are deemed a potential threat to public, animal, or plant health.
- Registration is part of the government's efforts to improve the ability of the US to prevent, prepare for, and respond to bioterrorism and other public health emergencies
- Required by law (42 CFR Part 73).

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What is the registration process and how does it cover select agent activities at UNMC?

- The UNMC Biosafety Officer is designated the Responsible Facility Official and has on behalf of the Institution, submitted an application to the CDC for registration.
- This application contains information on where work involving select agents is presently being conducted and the specific individuals approved to do work.
 - Any change to the original registration must be approved through a CDC application process

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What are the basic requirements for individuals who wish to handle and use these agents at UNMC?

- All individuals working with or having access to select agents or toxins must have an approved security risk assessment done.
- An evaluation of each individual is done to determine if the person is considered “restricted” based on the criteria of the USA PATRIOT Act.
- An extensive laboratory evaluation process will ensue prior to granting approval.

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Who is a “restricted person”?

- Under indictment for a crime punishable by imprisonment for a term > 1 year.
- Convicted of a crime punishable by imprisonment for a term > 1 year.
- Fugitive from justice
- Unlawful user of a controlled substance
- Alien illegally or unlawfully in the US
- Adjudicated as a mental defective or has been committed to a mental institution
- National of a country that the HHS Secretary has determined provides support for terrorism.
- Dishonorable discharge from the Armed Services

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What process must be followed to transfer and receive select agents or toxins?

- Both the recipient and the transferor must be registered with the CDC.
- Transfer requires the submission of an Form 2 with the CDC
 - Formerly called the EA-101 form
 - Form 2 is available from the biosafety officer
- The UNMC Biosafety Officer must complete the form and document the transfer on behalf of the Institution.

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What penalties can result by non-compliance to federal mandates concerning work with these agents?

- Violation of the Federal mandates can result in civil money penalties of \$250,000 for individuals and \$500,000 for the Institution, and/or imprisonment of up to 5 years.

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Working with Select Agents



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What laboratory safety standards do I need to apply to work with or possess select agents or toxins?

- Follow the requirements outlined in the following:
 - NIH/CDC Biosafety in Microbiology and Biomedical Laboratories (BMBL) manual.
 - NIH Guidelines for Research Involving Recombinant DNA Molecules
 - 29 CFR 1910.1450 and 1910.1200
- Submit an Institutional Biosafety Committee application

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What specific security requirements are necessary to work with or possess select agents?

- Specific components of a security plan must include:
 - inventory control procedures.
 - controlled access.
 - procedures for loss or compromise of keys, passwords, combinations, etc.
 - procedures for loss or theft, alteration of inventory records, etc.
 - measures to escort and monitor individuals not approved by a security risk assessment.

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What specific record-keeping requirements are necessary?

- The PI must maintain:
 - an up to date, accurate list of individuals approved to handle these agents.
 - an accurate inventory of each select agent and toxin to include:
 - name
 - characteristic
 - quantity
 - laboratory inspection records.
 - safety, security, and emergency response plans.
 - training records.
 - transfer documents and permits.



What penalties can result by non-compliance to federal mandates concerning work with these agents?

- Violation of the Federal mandates can result in civil money penalties of \$250,000 for individuals and \$500,000 for the Institution, and/or imprisonment of up to 5 years.

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Working with Select Agents and Toxins at UNMC / UNO

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What do I need to do to work with select agents or toxins on the UNMC / UNO campuses?

- Contact the Biosafety Officer to initiate the process of a security risk assessment.
- File an IBC proposal.
- Identify personnel in the laboratory who will need to have a security assessment.
- Develop laboratory security, safety, and emergency response plans.

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Conclusion

- Federal mandates that regulate the handling and possession of select agents and toxins must be followed.
- The Biosafety Officer will work with individual investigators to make sure that all provisions of the federal laws are followed.

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Conclusion continued

- Plan well in advance since this entire process for registration and assessment may take several months to complete!
- Under no circumstance will investigators be allowed to handle these agents without prior approval.

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This completes Module 3

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