



Compliance with the Select Agent Regulations

SNL Biosecurity Team

Principles of Laboratory Biosecurity Course

ABSA Summer Seminar Series

Albuquerque, NM

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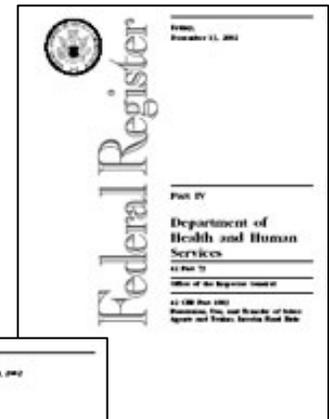
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New US Regulatory Environment for Biosecurity

- **USA PATRIOT Act of 2001 – US Public Law 107-55**
 - **Restricted Persons**
- **Bioterrorism Preparedness Act of 2002 – US Public Law 107-188**
 - **42 CFR 73 (Human and Overlap)**
 - **9 CFR 121 (Animal and Overlap)**
 - **7 CFR 331 (Plant)**
- **Hazardous Materials Transportation Security Requirements**
 - **49 CFR 172**





Public Health Security and Bioterrorism Preparedness and Response Act 2002

- **Implementing Codes of Federal Regulations (CFR) require specific measures:**
 - **Registration of a facility if they possess one of the 80 Select Agents**
 - **Security risk assessments for individuals with access to Select Agents**
 - **Facility must designate a Responsible Official**
 - **Security, safety and emergency response plans**
 - **Safety and security training**
 - **Regulation of transfers of Select Agents**
 - **Recordkeeping**
 - **Safety and security inspections**



Select Agents

- **Lists of agents that affect**
 - **Humans**
 - **Animals**
 - **Both humans and animals (zoonotic)**
 - **Plants**

- **Potential to cause substantial harm to**
 - **Human health**
 - **Animal or plant health**
 - **Animal or plant products**



Human Select Agents and Toxins

- **Cercopithecine herpesvirus 1 (Herpes B virus)**
- **Crimean-Congo haemorrhagic fever virus**
- **Ebola viruses**
- **Lassa fever virus**
- **Marburg virus**
- **Monkeypox virus**
- **South American Haemorrhagic Fever viruses (Junin, Machupo, Sabia, Flexal, Guanarito)**
- **Tick-borne encephalitis complex (flavi) viruses**
- **Variola major virus and Variola minor virus (Alastrim)**
- ***Coccidioides posadasii***
- ***Rickettsia prowazekii***
- ***Rickettsia rickettsii***
- ***Yersinia pestis***
- **Abrin**
- **Conotoxins**
- **Diacetoxyscirpenol**
- **Ricin**
- **Saxitoxin**
- **Tetrodotoxin**
- **Shiga-like ribosome inactivating proteins**



Overlap Select Agents and Toxins

- Eastern equine encephalitis virus
- Hendra virus
- Nipah virus
- Rift Valley fever virus
- Venezuelan equine encephalitis virus
- Botulinum neurotoxins
- *Clostridium perfringens* epsilon toxin
- Shigatoxin
- Staphylococcal enterotoxins
- T-2 toxin
- *Bacillus anthracis*
- Botulinum neurotoxin producing species of *Clostridium*
- *Brucella abortus*
- *Brucella melitensis*
- *Brucella suis*
- *Burkholderia mallei*
- *Burkholderia pseudomallei*
- *Coccidioides immitis*
- *Coxiella burnetii*
- *Francisella tularensis*



Animal Select Agents and Toxins

- African horse sickness virus
- African swine fever virus
- Akabane virus
- Avian influenza virus (highly pathogenic)
- Bluetongue virus (exotic)
- Pox viruses (camel, goat, sheep)
- Classical swine fever virus
- Foot and Mouth Disease virus
- Japanese encephalitis virus
- Lumpy skin disease virus
- Malignant catarrhal fever virus
- Menangle virus
- Newcastle disease virus (velogenic)
- Peste des petits ruminants virus
- Rinderpest virus
- Swine vesicular disease virus
- Vesicular stomatitis virus (exotic)
- *Cowdria ruminantium*
- *Mycoplasma capricolum*
- *Mycoplasma mycoides*
- Bovine spongiform encephalopathy agent



Plant Select Agents and Toxins

- ***Candidatus Liberobacter africanus***
- ***Candidatus Liberobacter asiaticus***
- ***Peronosclerospora philippinensis***
- ***Ralstonia solanacearum*, race 3, biovar 2**
- ***Sclerophthora rayssiae***
- ***Synchytrium endobioticum***
- ***Xanthomonas oryzae***
- ***Xylella fastidiosa***



Clinical / Diagnostic Specimen Exemption

- **Within 7 days of identification – destroy or transfer (unless otherwise directed by Administrator or HHS Secretary)**
- **Secure Select Agent from time of identification until transfer or destruction**
- **Report identification**
 - **Immediate reporting**
 - **African horse sickness virus, African swine fever virus, BSE, *Bacillus anthracis*, Bot toxins, *Brucella melitensis*, CSF, FMD, *Francisella tularensis*, Hendra, HPAI, Nipah, Newcastle, Rinderpest, RVF, swine vesicular disease virus, Variola major, Variola minor, VEE, VHFs, *Yersinia pestis*, all plant SA**
 - **All others within 7 days**
 - **May be less stringent requirements during outbreaks**



Registration

- **An “entity” (institution) is required to register**
 - **Responsible Official**
 - **List and location of Select Agents**
 - **Individuals requiring access to Select Agents**
- **Certificate valid only for specific agents, activities, and personnel**
 - **Modifications must be approved**
- **Certificate granted once all conditions of Rule are met**
- **Valid for 3 years**



Security Risk Assessment

- **Required for Responsible Official and persons owning the facility**
- **Required for individuals requiring access to Select Agents**
 - **Access = has possession or the ability to gain possession of a Select Agent**
 - **Work independently with Select Agents (e.g. Scientists)**
 - **Need independent access to areas where Select Agents can be easily obtained (e.g. Guards, Mechanical support)**
- **“Restricted Persons” cannot have access**
- **Approvals effective for 5 years**
- **Forms for personal information**
- **Fingerprints**
- **Dept. of Justice searches databases**
- **Expedited reviews may be requested**





Responsible Official (RO)

- Designated by institution
- Has authority and responsibility for institution's compliance with CFR
- Develops and implements
 - Safety plans
 - Security plans
 - Training
- Authorizes access to Select Agents by authorized personnel only
- Responsible for transfer of Select Agents to only approved individuals and institutions
- Reports loss, theft, release of agents and toxins
- Maintains records

RO is point-of-contact for all Select Agent regulatory activities



Security Plan

- **“Security plan must be designed according to a site-specific risk assessment and must provide graded protection in accordance with the risk of the select agent or toxin, given its intended use”**
- **Plan must be:**
 - Reviewed annually
 - Exercised annually
 - Reviewed and revised as necessary
 - After annual review, any drill, or incident





Select Agent Rule Security Plan Requirements

- Describe physical security, inventory control, and information systems control
- Describe access controls
- Describe provisions for routine cleaning, maintenance and repairs
- Establish procedures for removal of unauthorized or suspicious persons
- Describe procedures for lost or compromised keys, passwords, combinations, etc. and protocols for changing
- Describe procedures for reporting unauthorized or suspicious persons, activities, loss or theft, or alteration of records
- Ensure authorized individuals understand and comply with security
- <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5119a1.htm>



Minimum Security Plan Requirements

- SA are not stored or used in public areas
- Allow access only to DOJ-approved individuals
- Provide continuous escort by cleared individual for uncleared cleaning, maintenance and repair personnel
- SA storage areas (e.g. freezers, cabinets) have access controls
- Inspect all suspicious packages entering / leaving SA areas
- Protocol for transfer within institution
 - Including Chain of custody
- Mandates that authorized individuals do not share their access (e.g. card key, passwords)
- Report any compromises of security



Biosafety Now Part of Regulations

- **Biosafety and containment must be sufficient to contain the select agent**
- **Written biosafety plan**
 - **Commensurate with risk of the select agent**
 - **CFRs refer to:**
 - **BMBL – including all appendices**
 - **OSHA 29 CFR 1910.1200 (Hazard Communication)**
 - **OSHA 29 CFR 1910.1450 (Occupational Exposure to Hazardous Chemicals in Laboratories)**
 - **NIH Guidelines for Research Involving Recombinant DNA Molecules**
 - **Reviewed and revised annually**
 - **Exercised and evaluated annually**



Incident Response Plan

- **Facilities must develop and implement an incident response plan to include:**
 - **Definition of hazards of Select Agents**
 - **Coordination with responders**
 - **Lines of authority, communication, etc.**
 - **Security and control of site**
 - **Decontamination**
 - **Emergency notification and response**
 - **First aid and emergency medical treatment**





Training

- **Required for approved personnel and unapproved visitors**
- **Required before beginning work; annually thereafter**
- **Document that training was understood**
- **Security training program**
 - **Is based on institution's security plan and requirements of Select Agent work**
 - **Verifies understanding (test)**
 - **Can be internet-based**



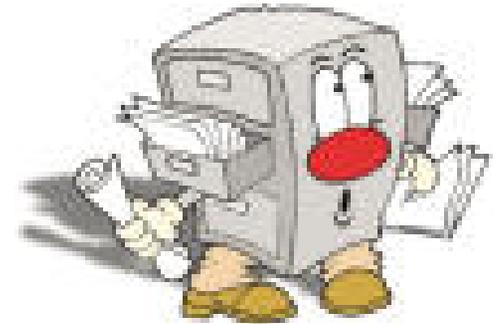
Transfers

- **Requirements for transfer within US**
 - **Sender must:**
 - Be registered
 - Or be a clinical (diagnostic) lab transferring to registered lab
 - **Recipient must:**
 - Be registered
 - Complete verification of receipt forms
 - Report if expected materials not received within 48 hours
 - **Report to HHS when destroyed or used up**
 - Amendment to Form 1



Records

- **List of approved individuals**
- **Accurate, current inventory**
- **Access to Select Agents**
- **Access to areas:**
 - **Name of individual**
 - **Date and time entered and left area**
 - **Name of individual who escorted unapproved individuals**





Inspections

- **HHS or USDA may inspect with or without cause**
- **Inspections are performed prior to certificate of registration (USDA)**
- **Inspections are part of registration (HHS); not required before certificate issued**
- **Examines facility safety, security, training, records, etc.**
 - **BMBL is cited in regulations**



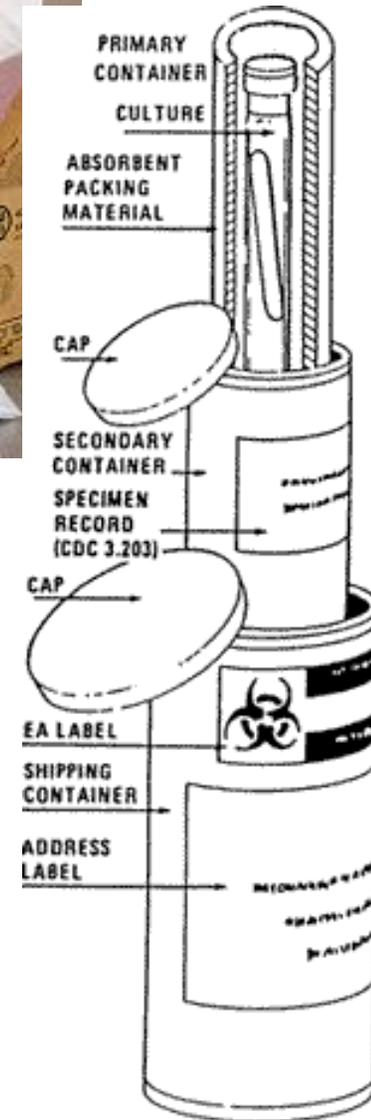
Select Agent Rule

Potential for Law Enforcement Engagement

- **Assistance with facility risk assessment**
 - **Insight into local threat environment**
- **Facility security plan and incident response plan must be performance tested**
 - **Participation in these tests might be helpful to both parties**
- **Theft, loss, or release must be reported to CDC/APHIS, and appropriate Federal, State, or local law enforcement agencies upon discovery**
 - **Reporting must include the list of Federal, State, or local law enforcement agencies to which the facility will report theft, loss, or release in order to facilitate a coordinated response**

Hazardous Material Transportation Regulations 49 CFR 100 - 185

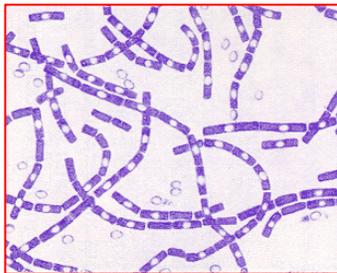
- Infectious substances (Class 6.2) and toxins (Class 6.1) are HazMat
- 49 CFR 172 (HM 232) mandates security measures for the transport of some HazMat
- Select Agents regulated under 42 CFR 73 require HazMat transport security measures
 - DOT will likely extend requirements to 9 CFR 121 and 7 CFR 331 agents



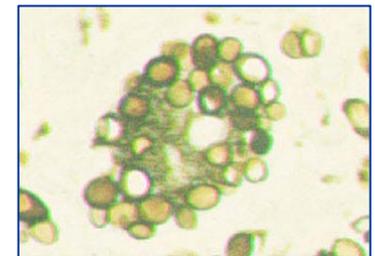


Transport Security Requirements

- **HazMat regulations security requirements include:**
 - **Training**
 - Security awareness training
 - Specific training as appropriate
 - **Written security plan**
 - Based on assessment of transportation security risks
 - Addresses personnel security, unauthorized access, en-route security



Bacillus anthracis



Coccidioides immitis



Conclusions

- **CFRs prescribe minimum security requirements**
- **CFRs mandate security plan based on a risk assessment**
- **Biosecurity elements under the CFRs can be discussed in context of earlier briefings:**
 - **Physical security**
 - **Personnel security**
 - **Material control & accountability**
 - **Transfer security**
 - **Information security**
 - **Program management**