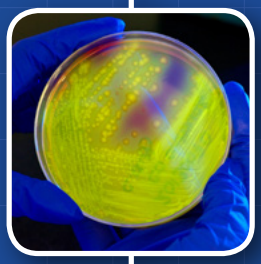

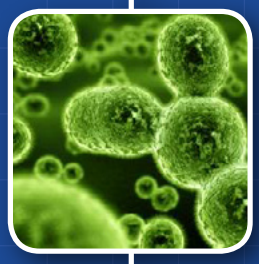

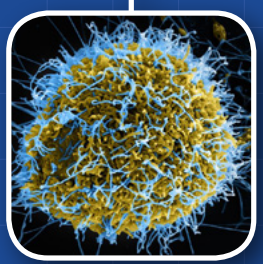

RESPONSIBLE OFFICIAL RESOURCE MANUAL

7 CFR Part 331, 9 CFR Part 121, 42 CFR Part 73

OCTOBER 2014

Centers for Disease Control and Prevention
Division of Select Agents and Toxins

Animal and Plant Health Inspection Service (APHIS)
Agriculture Select Agent Program

The Federal Select Agents Program (FSAP) Resource Manual for the Responsible Official was created to assist the Responsible Official (RO) and the alternate Responsible Official (ARO) in carrying out the duties and responsibilities as defined in the Select Agent Regulations. The information is not intended to specify a particular solution for meeting the regulatory requirements, but instead to provide suggestions, ideas and a range of possible solutions. The RO Resource Manual is a distillation of the expertise from the directors, inspectors and support personnel of FSAP and the many interactions with entity responsible officials, principal investigators, biosafety officers, security officers, engineers, subject matter experts, and government agency officials.

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PREFACE

The Federal Select Agents Program (FSAP) Resource Manual for the Responsible Official was created to assist the Responsible Official (RO) and the alternate Responsible Official (ARO) in carrying out the duties and responsibilities as defined in the Select Agent Regulations. The information is not intended to specify a particular solution for meeting the regulatory requirements, but instead to provide suggestions, ideas and a range of possible solutions. For the experienced RO or ARO we hope that this manual will be a valuable resource that assists them in carrying out their very important responsibilities. For the new RO or ARO, we hope that this manual will be helpful in quickly gaining a comprehensive understanding of the Select Agent Regulations and the responsibilities of their position. Most of the information in this manual is available on the FSAP web site www.selectagents.gov but we believe that making the information available in one collection will enhance the usefulness and availability of the information. We recognize that every entity is different and not every situation will be addressed, or every question will be answered. It is for that reason that we emphasis the critical importance of maintaining frequent communication between the RO/ARO and the FSAP. Active communication between the entity and the FSAP cannot be too strongly emphasized.

The information contained in this manual is for guidance purposes only. It is not regulatory and does not have the force and effect of law. The select agent regulations are set forth in 42 CFR Part 73, 9 CFR Part 121 and 7 CFR Part 331. If you have questions or concerns about compliance with the Select Agent Regulations please contact the FSAP.

The purpose of the FSAP is to ensure that select agents and toxins are handled safely and securely and this assurance involves the implementation, monitoring and enforcement of the Select Agent and Toxins Regulations. In carrying out this purpose, the FSAP serves to protect the humans, animals and plants from those individuals or groups that would seek to use biological agents and toxins in such a way as to place human, animal, and plant health at risk. The objective of this resource manual is to promote biological laboratory biosafety and security by providing the RO and ARO with knowledge and tools useful to ensure compliance with the Select Agent and Toxin Regulations.

In addition to serving as a general resource, this manual can also be used for self-study as well as a resource for the select agent training requirements. The general format of the chapters is to explain the regulatory requirements to enhance the RO's understanding and to provide the appropriate resource or guidance to assist the RO in ways that the requirements can be met. The resources and guidance documents are provided in the appendix. The chapters can be approached in the order they are presented or the RO/ARO may choose to focus on chapters of primary interest first.

The Quick Reference to the Federal Select Agent Program that follows this chapter is intended to give an overview of the FSAP. For the new RO or ARO this quick reference can serve as a snap shot of what is required of an entity. From this reference the RO/ARO can go to the particular chapter for a more comprehensive treatment of the subject.

The first chapter is an introduction to the FSAP and includes the history of the program and references the laws, regulations, and guidelines that are used by the program. This chapter is followed by a description of the duties and responsibilities of the RO and ARO. We suggest reading this chapter at the beginning, especially for the new RO or ARO, because it helps to put the other chapters in perspective. The next chapter provides procedures for registering with the FSAP and how to amend an entity registration. Reporting requirements are

covered in Chapter 4. Chapter 5 covers transfer of select agents and toxins and the procedures for obtaining approval prior to the transfer. The next three chapters cover biosafety and the biosafety plan, security and the security plan and incident response requirements and the incident response plan. Chapter 9 contains a description of restricted experiments and covers procedures on how to request approval to conduct restricted type experiments. Also included in this chapter are procedures for requesting exemptions and exclusions. Chapter 10 provides information on the records that must be maintained. Chapter 11 describes the training that an entity must provide to the staff and visitors. In chapter 12 drills and exercises are described and suggestions on how to conduct them. The FSAP inspection process is described in Chapter 13. This is a chapter that the RO/ARO may want to review prior to a scheduled FSAP inspection. If you have never experienced a FSAP inspection this will be helpful in preparing for the inspection. Chapter 14 provides information on commissioning and verification of containment facilities.

While the focus of this manual is on the Federal Select Agent Program, the information may also be of value in an institution's biosafety and security program. The requirements for safety, security, and incident response in the regulations are those that every institution working with infectious disease agents and biological toxins should consider in creating their safety and security programs. It is true that safety and security programs have costs; however, they do serve to protect the institution against the risk of loss of the ability to carry out the mission of the institution. Incidents of exposure, disruption of work, damage to facilities, and other situations may put the institution at risk of legal challenges and loss of credibility in the community.

An effort has been made to keep acronyms to a minimum. The most common acronyms found in this manual are as follows:

ARO – alternate Responsible Official
BSAT – Biological Select Agent and Toxin
FSAP – Federal Select Agent Program
RO – Responsible Official
SRA – Security Risk Assessment
CDC/DSAT – Centers for Disease Control and Prevention/Division of Select Agents and Toxins
APHIS/AgSAS – Animal and Plant Health Inspection Service/Agricultural Select Agent Services

The editor and the reviewers of this manual have combined their expertise to create a resource intended to assist the Responsible Official and alternate Responsible Official in performing the responsibilities of their position. This is a living document and will be continually updated as changes require. We hope this manual will fulfill the purpose for which it is intended and we encourage those who use it to contact the editor if there are errors or where clarification is required, and to provide comments on how to make the manual better.

HOW TO USE THE MANUAL

There are several ways to use this manual and how you decide to use it depends on what you wish to gain from the information provided, how much time you have to devote to the effort, the kind of learning experience that works for you and what you determine to be the value of your experience with the manual. Some of the ways the manual might be used are listed as follows:

As a Reference: The manual can serve as a reference. It is a source of information that you can refer to when questions come up about select agents and toxins. This approach is one that may work best for the seasoned RO/ARO who occasionally needs to review their knowledge about a particular subject. The manual will be updated periodically as changes occur in the FSAP. The RO/ARO will receive the updates as they are made, but as stated in the Preface not every situation or issue will be addressed and communication with the FSAP is your most valuable reference.

For Self-Study: Another use of the manual is for the person who wants to study the content of the manual, but prefers to do so at their own pace and in their own order of subjects. This may be appropriate for the RO or ARO who has just been appointed to their position. Each chapter begins with a learning assistant statement which is represented by this symbol. The learning assistant states the study objectives for the chapter and will reference an exam that you can take after you have completed the chapter to determine how much of the information was understood and identify any parts that you should revisit. Self-Evaluation exams for each chapter are provided in Appendix AK.

Also you may see a symbol that looks like this: This will indicate that there are additional resources that you may want to reference for more information on the subject.

Staff Training: Part of the RO/ARO responsibilities is to ensure that the entity staff is provided initial and refresher training on FSAP security, incident response, and safety requirements. This manual is not intended to serve as a training program for entity staff, but the RO/ARO may find some of the content in the manual useful in developing entity staff training on the select agent requirements.

For the convenience of the users of this manual we have placed the contents of the manual on a computer disk that contains a file of the chapters and separate appendix files. The user of the manual may choose to load the disk into their computer system or use the disk to access the documents. The manual is in Adobe format and requires an Adobe reader. Periodically updates to the manual will be provided and the user should remove the out of date files and replace them with the updated files.

THE FEDERAL SELECT AGENT PROGRAM: A QUICK REFERENCE

This is a quick reference for those who are not familiar with the Federal Select Agent Program (FSAP) and those that need a quick reminder. This reference is not inclusive of all that a person needs to know about the FSAP. Chapters, and Appendixes in this manual, where more extensive information can be found, are listed. For specific questions, concerns or issues, or for information not contained in this manual, please contact the Federal Select Agent Program at LRSAT@cdc.gov, or AgSAS@aphis.usda.gov, 404-718-2000 (DSAT Tel.), 404-718-2096 (DSAT Fax) or 301-851-3300 (Option 3) (AgSAS Tel.) or 301-734-3652 (APHIS Fax) or go to the Program web site.

Federal Select Agent Program (FSAP)

The Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (Public Law 107-188) (the Act) authorizes the Secretaries of HHS and the USDA to regulate the possession, use, and transfer of biological agents and toxins that they determine have the potential to pose a severe threat to public health and safety, animal or plant health, or animal or plant products (select agents and toxins). The Centers for Disease Control and Prevention's Division of Select Agents and Toxins and the USDA Animal and Plant Health Inspection Service (APHIS), Agricultural Select Agent Services (AgSAS) are jointly charged with implementing this oversight of select agents and toxins. This joint effort constitutes the Federal Select Agent Program. Any individual or entity that possesses, uses and/or transfers a select agent or toxin must be registered with the FSAP and must comply with the Select Agent Regulations. (Chapter 1 and 3)

Resources:

Select Agents and Toxins List
Select Agent and Toxin Exclusions
Permissible Toxin Amounts
Select Agents Regulations
Select Agent Forms

Responsible Official

The Responsible Official (RO) is the individual at the entity who is accountable for entity compliance with the Select Agent Regulations. The RO must be approved by the FSAP, be familiar with the regulations, have the authority to act on behalf of the entity, maintain the required records, and conduct annual inspections. The Alternate Responsible Official (ARO) is a person appointed by the entity to serve as the RO when the RO is not available. An ARO must be able to meet all of the requirements of being an RO. An entity may appoint more than one ARO. The entity is not required to have an ARO, but it is highly recommended. (Chapter 2)

Resources:

Three Year Cycle of RO Tasks
Responsible Official Guidance Document

Select Agents and Toxins

There are a total of 65 select agents and toxins: 34 HHS only, 10 Overlap, 14 Veterinary and 7 Plant pathogens. HHS Only agents are hazardous to humans, Overlap agents are hazardous to both humans and animals, USDA agents, veterinary and plant pathogens, are hazardous to animals and plants and animal and plant products. Toxins in quantities below a specified amount listed in the regulations are not subject to the Select Agent Regulations. Some of the criteria used for determining whether an agent or toxin is placed on the HHS list include the effect on human health, the degree of contagiousness of the agent or potency of the toxin, the methods by which it is transferred to humans and the availability

and effectiveness of pharmacotherapies and immunizations to treat and prevent any illness. For USDA pathogens, some of the criteria considered include the effect of an agent on animal or plant health or products, the virulence of an agent, the method of transfer to animals or plants, and the availability and effectiveness of medicines and vaccines to treat and prevent illness.

Resource:

Select Agents and Toxins List

Registering with the FSAP

Entities that are required to register with the FSAP because they wish to possess, use and transfer select agents and toxins should contact the FSAP about the requirements for registration. Entities should ensure that they have facilities that are operational and should complete and submit an APHIS/CDC Form 1. The form and guidance on completing the form is provided on the FSAP web site. The registration process takes approximately 4 – 6 months depending on the size and complexity of the entity and the operational readiness of the facilities. An inspection by the FSAP is conducted prior to registration and a registration certificate is issued for a period of up to three years. Entities that wish to possess HHS only agents should submit the application to the CDC/DSAT. Entities that wish to possess only USDA pathogens should submit the application to APHIS/AgSAS. Entities that wish to possess both HHS only and USDA only, or Overlap agents, may submit their application to either APHIS/AgSAS or CDC/DSAT. (Chapter 3)

Resources:

Select Agents and Toxins List
Select Agent and Toxin Exclusions
Permissible Toxin Amounts
Select Agents Regulations
Registration for Possession, Use, and Transfer of Select Agents and Toxins

Security Risk Assessment

Every individual at the entity that is listed on the entity registration form as requiring access to select agents and toxins is required to have a security risk assessment (SRA). To obtain a SRA an individual must submit the Federal Bureau of Investigation (FBI) form FD 961 and fingerprints cards to the Criminal Justice Information Service (CJIS). The SRA process normally takes less than 30 days once all of the information is received by the CJIS from the individual requiring access. (Chapter 7)

Amending the Registration

A registered entity must advise the FSAP using the amendment process anytime there are changes in personnel that have been listed on the registration form, any time the entity wishes to acquire additional select agents or toxins or remove select agents and toxins from registration, and any time there are changes in work objectives or modifications to the facility. (Chapter 3)

Resource:

Registration for Possession, Use, and Transfer of Select Agents and Toxins

Inspections

The FSAP conducts on-site inspections to confirm entity compliance with the Select Agent Regulations. Initial and renewal inspections are scheduled with the entity. Verification or compliance inspections may occur at any time and may be announced or unannounced. The inspection consists of a review of the facilities and the support services; interviews of personnel; review of the biosafety; security and incident response plans; audit of the inventory; review of training; and access, transfer, and equipment maintenance records. A report of the inspection is normally provided to the entity within 21 days after the conclusion of the inspection and the entity is required to respond to any deficiencies listed in the report within 14 days of receipt of the report. One

way that the RO can prepare for an inspection is by conducting an internal audit using the inspection checklists found on the FSAP web site. (Chapter 13)

Resources:

Inspection Checklists
Inspection Video

Biosafety

Each registered entity must have a biosafety plan and the plan must describe the procedures for mitigating the risks of the agents and toxins and the work performed. The Biosafety in Microbiological and Biomedical Laboratories, 5th Edition contains biological standards. The OSHA Laboratory Standard (29 CFR 1910) contain regulations regarding exposure to chemicals. The NIH Guidelines contain standards for working with recombinant DNA molecules. These are excellent resources for developing the entity biosafety plan. It is important that entities review their biosafety plans at least annually and make any necessary revisions, especially if there have been changes in the facilities, agents, or work objectives. (Chapter 6)

Resources:

Biosafety in Microbiological and Biomedical Laboratories
NIH Guidelines for Research Involving Recombinant DNA Molecules
Occupational Safety and Health Administration Regulations

Security

Each registered entity must have a written security plan that is based on a security risk assessment. The security plan and the entity physical security must be capable of ensuring the security of the select agents and toxins possessed by the entity. Entities that have Tier 1 agents are expected to have enhanced security and this must be described in the plan. The Select Agent Regulations list the components that are expected to be part of the entity's program for ensuring the security of the select agents and toxins. (Chapter 7)

Resources:

Guidance for Suitability Assessments
Information Systems Security Control Guidance Document
Security Guidance for Select Agent or Toxin Facilities
Security Risk Assessments Tool

Incident Response Plan

Each registered entity must have a written incident response plan that describes the procedures for responding to emergency situations. Examples of situations that should be covered are a spill in the laboratory, power outage, bomb threat, and natural or man-made hazards. Coordination with local emergency responders should be part of the plan. (Chapter 8)

Resource:

Incident Response Plan Guidance Document

Occupational Health

Each registered entity is expected to have policies and procedures for handling exposures or potential exposures to select agents and toxins and to describe this in either the incident response plan or the biosafety plan. The employees should be advised on the symptoms of infection or intoxication with the select agents and toxins and how to obtain medical care if needed. Entities with Tier 1 agents are expected to have an occupational health plan. (Chapter 8)

Resource:

Occupational Health Program Guidance Document for Working with Tier 1 Select Agents and Toxins

Transfers

FSAP approval to transfer select agents and toxins from one registered entity to another registered entity is required prior to transfer. The request for approval should be submitted to either the CDC/DSAT or the USDA/APHIS using the APHIS/CDC Form 2. Approval usually takes 2-3 business days and the transfer approval is valid for 30 days. The Department of Transportation regulations should be consulted in regards to packaging agents and toxins for shipment. (Chapter 5)

Resource:

Request to Transfer Select Agents and Toxins

Theft/Loss/Release Reporting

Registered entities are required to report immediately by e-mail, telephone, or fax any theft, loss, or release of a select agent or toxin and this must be followed by submitting an APHIS/CDC Form 3 to either CDC/DSAT or USDA/APHIS within 7 days. Entities that are not registered with the program, such as a diagnostic laboratory, which have a theft, loss, or release are required to report as well. (Chapter 4)

Resource:

Report of Theft, Loss, or Release of Select Agents and Toxins

Diagnostic Reporting

Registered entities are required to report the isolation of a confirmed select agent or toxin within 7 days using the APHIS/CDC Form 4. There are some select agents that require immediate notification with a follow-up report within 7 days. Non-registered entities are required to report agents or toxins that have been confirmed as a select agent or toxin. Unless directed otherwise by the FSAP non-registered entities are required to destroy or transfer any confirmed select agent or toxin within seven days of confirmation. (Chapter 4)

Resource:

Report of the Identification of a Select Agent or Toxin

Restricted Experiments

Experiments involving the transfer of drug resistance to a select agent that is not known to acquire the trait naturally if it could compromise the control of the agent, and experiments that result in recombinant DNA or synthetic nucleic acid containing genes capable of producing select agent toxin lethal for vertebrates at an LD50<100 ng/kg body weight require prior approval by the FSAP. (Chapter 9)

Resource:

Restricted Experiment Guidance

Exclusions and Exemptions

Exemptions refer to specific situations cited in the Select Agent Regulations where the Select Agent Regulations do not apply. An example is a diagnostic laboratory that isolates and confirms a select agent. The laboratory is exempted from having to register with the FSAP as long as they report the select agent to the FSAP and they destroy or transfer the agent. Another example of an exemption is where a select agent is part of an FDA approved product such as toxin used for cosmetic purposes. Exclusions include strains of select agents that are attenuated and do not pose a hazard to human health or animal and plant health. An entity that has an excluded strain is not required to register the excluded strain. An example of an excluded agent is the Sterne strain of *Bacillus anthracis* that is devoid of plasmids pX02. There is a list of excluded strains on the FSAP web site. (Chapter 9)

Resources:

Select Agent and Toxin Exclusions
Permissible Toxin Amounts

Drills and Exercises

Registered entities are required to conduct drills or exercises to test their biosafety, security, and incident response plans. Drills and exercises can also be excellent formats for meeting the staff training requirements. The drill or exercise should involve everyone who is responsible for responding to the situation. Drills for responding to a suspicious package that arrives on the loading dock (security), drills for responding to the escape of an infected animal from containment (biosafety), or an exercise on activities before and after a flood (incident response/security/biosafety) are examples of the kind of drills or exercises that might be conducted. The results of the drill or exercise should be incorporated into changes in entity policies, or plans as appropriate. (Chapter 12)

Training

Registered entities must provide information and training to individuals who have access to select agents and toxins on biosafety, security and incident response. Security awareness training must be provided by those entities that have Tier 1 agents. The training must be conducted at least annually and it must be documented. The training should be structured to meet the needs of the individual based on the work they do, the agents they work with and the risks. (Chapter 11)

Resource:

Guidance for Meeting Training Requirements of the Select Agent Regulations

Hotline

To provide a mechanism for individuals to report safety, security, or other concerns associated with select agents and toxins, the Department of Health and Humans Services (DHHS), Office of Inspector General (OIG) maintains a hotline which offers a confidential means for reporting this vital information. When reporting these issues to the OIG it is important to indicate that it is a "Select Agent Program" issue. The contact information is 1-800-447-8477 (Tel) or 1-800-223-8164 (Fax).

Resource:

OIG Hotline Operations

CHAPTER 1: THE FEDERAL SELECT AGENT PROGRAM

OBJECTIVE: Acquire an understanding of the history of the Federal Select Agent Program (FSAP), why it was created and how the FSAP is designed to carry out the Select Agent Regulations.

For self-study it is recommended that you take the Self-Evaluation Exam after you have completed reading the chapter. Compare your answers with the answers provided and review any areas were you did not provide the correct answers.

History of the FSAP

Congress Acts to Deter Bioterrorism

Establishment of Oversight of Select Agents

In 1995, an alleged neo-Nazi extremist and microbiologist was arrested for illegally obtaining *Yersina pestis* by mail order in the United States. Shortly thereafter Congress passed and the President signed into law section 511 of the *Antiterrorism and Effective Death Penalty Act of 1996* due to heightened concern about the ease with which disease causing agents could be obtained illegally. Prior to this action, there was no specific licensing, registration, or safety requirements for laboratories or individuals engaged in the transfer of human disease causing biological agents or toxins within the United States, and no Federal requirements to report the transfer of these agents or toxins. The 1996 legislation directed the Department of Health and Humans Services (HHS) to establish a list of biological agents and toxins that had the potential to pose a severe threat to public health and safety, implement regulations governing the transfer of these agents and toxins, and establish safety requirements for entities receiving these "select agents and toxins." This led to the establishment of the Laboratory Registration and Select Agent Transfer Program at the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia.

Following the events of September and October 2001, Congress significantly strengthened oversight of biological select agents and toxins (BSAT) with the passage of the *Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism Act of 2001* (USA PATRIOT Act), and *the Public Health Security and Bioterrorism Preparedness and Response Act of 2002* (The Bioterrorism Response Act). The USA PATRIOT Act restricted who could legally have access to a biological select agent or toxin (BSAT). Subtitle A of Title II of the Bioterrorism Response Act strengthened the HHS regulatory authorities over BSAT. Subpart B of Title II of The Bioterrorism Response Act (also called the Agricultural Bioterrorism Protection Act of 2002) granted comparable regulatory authority to the United States Department of Agriculture (USDA) for biological agents and toxins that have the potential to pose a severe threat to plant or animal health or plant and animal products. Subtitle C of the Bioterrorism Response Act required that USDA and HHS coordinate activities in regards to those agents and toxins that would be regulated by both agencies. These agents are defined as Overlap agents, which are zoonotic agents that have the potential to pose a severe threat to public health and safety as well as animal health. The Bioterrorism Response Act requires HHS and USDA to coordinate the regulation and oversight of entities with overlap agents and toxins including providing the entity with the choice of submitting the application for an Overlap agent to either USDA or HHS. These two agencies are required to coordinate the review of the registration application and obtain the concurrence of the other agency regardless to which agency the application is submitted. This coordination of registration and oversight by USDA and HHS has continued to this day and is an integral part of the Federal Select Agent Program. The Federal Select Agent Program (FSAP) is administered jointly by the CDC Division of Select Agents and Toxins (DSAT)

and the USDA Animal and Plant Health Inspection Services (APHIS) Agriculture Select Agent Services (AgSAS).

The BSAT Regulations

DSAT and the AgSAS fulfill their responsibilities under the Bioterrorism Response Act through the promulgation of three sets of regulations (42 CFR Part 73, 7 CFR Part 331, 9 CFR Part 121) that were initially published in the Federal Register on December 13, 2002. These regulations have been amended since their promulgation, with the last amendment being published in the *Federal Register* on October 5, 2012.

DSAT regulates biological agents and toxins that have the potential to pose a severe threat to public health and safety (42 CFR Part 73). AgSAS regulates biological agents that have the potential to pose a severe threat to plants and plant products (7 CFR Part 331) and agents that pose a severe threat to animals and animal products (9 CFR Part 121). The regulation of Overlap biological select agents that pose a severe threat to both humans and animals and animal products is addressed by both DSAT and AgSAS in 42 CFR Part 73 and 9 CFR Part 121. The FSAP promotes laboratory safety and security by developing, implementing, and enforcing the select agent regulations; providing guidance to the regulated community; and inspecting facilities where work with biological select agents and toxins is conducted.

Additional Regulations and Standards

In addition to the BSAT regulations mentioned above there are additional resources used by the FSAP to evaluate the security and safety of a laboratory possessing, using, and transferring BSAT:

- 29 C.F.R. Parts 1910.1200 (OSHA, Hazard Communication),
- 29 C.F.R Parts 1010.1450 (OSHA, Occupational exposure to hazardous chemicals in laboratories),
- 29 C.F.R. 1910.1030 (OSHA, Bloodborne pathogens),
- The National Institutes of Health (NIH) Guidelines for Research Involving Recombinant DNA Molecules is used for evaluating laboratories conducting recombinant research with select agents, and
- The Biosafety in Microbiological and Biomedical Laboratories, 5th Edition (BMBL) is the primary standard used by the FSAP to evaluate laboratory biosafety.

Development of the List of Select Agents and Toxins

In determining whether to regulate a biological agent or toxin the Bioterrorism Response Acts require that HHS and USDA consider the following criteria:

- The effect on human, animal or plant health after exposure to the agent or toxin;
- The effect on agriculture or agricultural products of a release of an agent or toxin;
- The infectivity and means of transmission of the agent or toxin to humans, animals or plants;
- The availability and effectiveness of pharmacotherapies, and immunizations and other control measures to treat and prevent any illness resulting from infections by the agent or toxin; and
- Any other criteria that the HHS or USDA Secretaries deem appropriate.

There are currently 65 select agents and toxins that are regulated. 34 biological agents and toxins are regulated by CDC and are referred to as HHS only

agents. Ten biological agents are listed by both HHS and USDA as "Overlap" and are regulated by both APHIS/AgSAS and CDC/DSAT because they can cause disease in both animals and humans. Twenty-one biological agents are regulated by APHIS and are referred to as "USDA Only" agents. The USDA Only agents include seven plant pathogens. The list of agents must be reviewed by the Federal Select Agent Program every two years and any proposed changes published in the Federal Register. Appendix B contains a list of all biological agents and toxins that are regulated.

Security Risk Assessments

The FBI's Criminal Justice Information Services (CJIS) conducts electronic records checks to identify those individuals who may be prohibited from possession or having access to select agents and toxins because they meet any of the prohibitors identified in section 175b of title 18, United States Coder or any of the restrictors listed in the Bioterrorism Response Act. The CJIS process of screening an individual is called a "Security Risk Assessment" (SRA). CJIS conducts security risk assessments of all individuals, Responsible Officials, Alternate Responsible Officials and non-governmental entities that apply to possess or request access to select agents and toxins. The Federal Select Agent Program authorizes possession of or access to select agents and toxins based in part on the results of the security risk assessment. Chapter 7 describes the SRA process and information on SRAs can be found on the Federal Select Agent Program web site.

Registered Entities

As of January 2013 there were 323 entities registered with the DSAT and 69 entities registered with AgSAS. Information on all entities is maintained in a common FSAP database. Approximately 11,000 individuals have an active SRA. The individual SRA is valid for a maximum of three years.

Regulatory Oversight

DSAT and AgSAS ensure compliance with the select agent regulations by inspecting entities to confirm that the entities have the appropriate security and safety measures in place to prevent theft, loss, or release of BSAT. While entities may register with either DSAT or AgSAS and can be inspected by either, in practice many inspections are conducted jointly by DSAT and AgSAS. During the onsite inspection the inspectors examine the rooms where BSAT are used and stored, review the entity biosafety, security and incident response plans, review training records, conduct employee interviews, conduct inventory audits, review access records, review drill/exercise activity and review the entity's physical security. Non-compliant entities that fail to come into compliance may have their registration suspended or revoked and may be subject to criminal or civil money penalties.

Interagency Coordination

Presidential Executive Order 13546 of July 2010, "Optimizing the Security of Biological Select Agents and Toxins in the United States", encouraged the FSAP to share information and conduct joint entity inspections with other governmental agencies (e.g., Department of Homeland Security, Department of Defense, Environmental Protection Agency, Veterans Administration and Department of Energy) of entities where those agencies have a vested interest, i.e. they either own the entity or fund the work performed at the entity. This is an important collaboration that advances the nation's overall terrorism deterrence strategy.

Changes to the Regulations

The FSAP is required to review biennially the list of regulated biological agents and toxins to determine if changes need to be made to the list. The changes may involve elimination of agents or toxins from the list, changes in the designation (HHS, USDA, Overlap) of the agents, and addition of agents or toxins to the list.

Presidential Executive Order 13486 of January 9, 2009, "Strengthening Laboratory Biosecurity in the United States" created a panel of representatives from government agencies to advise the President on ways to increase security at biological laboratories. Presidential Executive Order 13546 of July 2, 2010, "Optimizing the Security of Biological Select Agents and Toxins in the United States," addressed specific security issues and resulted in the amendments to the Select Agent Regulations. The proposed regulatory amendments were published for public comment on October 3, 2011 (76 FR 61206) with the final rule being published in the *Federal Register* on October 5, 2012 (77 FR 61084).

The HHS Inspector General, the USDA Inspector General, and the U.S. Government Accountability Office periodically evaluate FSAP practices and procedures and make recommendations to the HHS, USDA Secretary and to members of Congress respectively.

Outreach Program

The Federal Select Agent Program conducts an active outreach effort that involves providing information resources, guidance, information alerts, and workshops to assist the regulated community in complying with the Select Agent Regulations. Guidance developed by the FSAP includes a security plan template, inspection checklists, guidance on theft, loss and release, training, Responsible Official responsibility, security, incident response, suitability assessment, information systems security, working with Tier 1 agents, and video presentation on the entity inspection process. The FSAP website provides a resource for regulated entities and the public seeking information about the FSAP. Most of these resources are also provided as links in this manual.

Chapter 1 Quiz

CHAPTER 2: RESPONSIBILITIES OF THE RESPONSIBLE OFFICIAL

OBJECTIVE: Acquire an understanding of the duties and responsibilities of the Responsible Official.

For self-study it is recommended that you take the Self-Evaluation Exam for Chapter 2 after you have completed reading the chapter. Compare your answers with the answers provided and review any areas where you did not provide the correct answers.

"Responsible Official Guidance Document" is a good resource for the new RO or ARO as it provides a description of the duties and responsibilities of the position. It can also be helpful to the seasoned RO and ARO in reminding them of the requirements. The "Three Year Cycle of Tasks for the Responsible Official" may be helpful as a check list for the RO over the period of a three-year registration cycle.

Introduction

Each entity that is required to register under the Select Agent Regulations for the possession, use, or transfer of biological select agents and toxins (BSAT) is required to designate an individual as the Responsible Official (RO) and submit that person's name to the Federal Select Agent Program (FSAP), either the Centers for Disease Control and Prevention (CDC) Division of Select Agents and Toxins (DSAT) or the United State Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS), Agriculture Select Agent Program (AgSAS) for approval. This requirement is found in 42 CFR §73.9, 9 CFR §121.9 and 7 CFR §331.9 but the RO should be aware that there are other parts of the regulations that include RO responsibilities. While compliance with the Select Agent Regulations is ultimately the responsibility of the registered entity, the RO plays an essential role to ensure that his or her entity is in compliance with the Select Agent Regulations and serves as the main point of contact for all select agent registration, reporting, and compliance issues.

Fundamental Responsibilities of the Responsible Official

The RO is the individual identified by the registered entity as having the authority and responsibility to act on behalf of the entity to ensure compliance with the Select Agent Regulations. There can be only one RO at a registered entity at any given time. The core responsibilities of, and criteria to be, an RO are listed below:

- The RO must have passed a security risk assessment (SRA) conducted by the Federal Bureau of Investigation (FBI), Criminal Justice Information Services (CJIS) and be approved by the FSAP.
- The RO must be familiar with the select agent regulations to the extent that the RO can ensure that his or her entity is compliant with all of the requirements of the select agent regulations.
- The registered entity must not only assign the RO the responsibility to ensure compliance with the select agent regulations, the entity must also ensure that it delegates to the RO sufficient authority to speak and act on behalf of the entity. A registered entity which fails to vest in its RO sufficient authority to ensure compliance with all of the requirements of the select agent regulations has failed in one of its primary responsibilities.
- The RO must ensure compliance with the select agent regulations.
- The RO must ensure that annual inspections

are conducted for each laboratory and all other registered areas where select agents or toxins are stored or used in order to determine compliance with the requirements of the select agent regulations. The results of each inspection must be documented, and any deficiencies identified during an inspection must be corrected.

- The RO must have a physical (and not merely a telephonic or audio/visual) presence at the registered entity to ensure that the entity is in compliance with the select agent regulations and be able respond in a timely manner to onsite incidents involving select agents and toxins in accordance with the entity's incident response plan.

Designation of Responsible Official

The registered entity, as a part of its initial registration with the FSAP, must submit the name of the RO (and any ARO's) on the CDC/APHIS Form 1. The FSAP may also request that a current résumé or curriculum vitae for the RO be submitted as well.

The RO will need to foster open lines of communication with upper management, facility directors, principal investigators, veterinarians, contractors, local authorities and institutional oversight committees in order to manage a successful program compliant with the select agent regulations. The RO should be engaged in and be knowledgeable about the programs and operations of his or her entity. To the extent possible, an entity should avoid designating an owner, controller, or principal investigator as the RO as this arrangement may present conflict-of-interest situations. Nevertheless, the FSAP recognizes there are situations (e.g., small entities with limited personnel), in which this scenario may be unavoidable. Based on our experience with many types of entities, the RO position is a full time endeavor and requires much more time than what a principal investigator or owner can provide. Although it is not a violation of the select agent regulations for an individual serving as an RO to have other responsibilities, the FSAP would not recommend this especially at institutions with large and/or complex select agent programs.

When there is an anticipated change in an RO, the entity should submit the appropriate sections of APHIS/CDC Form 1 as early as possible to request approval of the new RO. The approval should be received before the current RO vacates the assignment as it is a requirement of the select agent regulations for a registered entity to have a RO approved by the FSAP at all times. This is not a lengthy process if the successor has a current security risk assessment. However, the entity should anticipate that for an individual without a current security risk assessment, approximately 45-60 days may be required for CJIS to conduct the electronic records check after submission of the appropriate documents to the CJIS (i.e., Form FD-961 and two fingerprint cards). The RO for an entity with Tier 1 BSAT must also have undergone the entity's suitability assessment process. This process also needs to be considered during RO transitions if the entity finds itself without an RO.

The ARO assumes the position and responsibilities of the RO either permanently or temporarily until a replacement is selected by the entity or the RO assumes full duties. The ARO must be able and willing to assume the full range of responsibilities of the RO. The entity would need only to submit an amendment to the APHIS/CDC Form 1 noting a permanent change.

Any time the FSAP determines an RO has not, or is not, fulfilling his or her responsibilities to ensure compliance with the requirements of the select agent regulations, the FSAP has authority to suspend, revoke or deny an entity's certificate of registration.

Designation of an Alternate Responsible Official

The regulations in Section 9(b) require that an entity may designate one or more individuals to be an ARO, who may act for the RO in his/her absence. Although it is not a requirement in the select agent regulations for an entity to designate an ARO, situations arise in which the RO is not available to provide appropriate regulatory oversight (e.g., vacation, protracted illness or extended travel). Therefore, it is advisable for the registered entity to designate one or more AROs to be available to act in the absence of the RO on a short-term, temporary basis. These individuals must have the knowledge and authority to ensure compliance with the select agent regulations when acting as the RO and be able to take appropriate action on behalf of the entity. Like the RO, an individual designated to serve as an ARO must be designated as an ARO on APHIS/CDC Form 1, have an SRA conducted by CJIS with a status of "Unrestricted," and be approved for the role by the FSAP.

However, as noted above, it is not consistent with the select agent regulations for the ARO to fulfill the responsibility and final decision-making of the RO when the RO is available to carry out his or her day–to-day responsibilities. In other words, the RO cannot delegate final decision-making responsibility to an ARO when the RO is physically present at the entity and able to carry out his or her responsibilities.

The RO may delegate authority to an ARO, or others in the program, for a wide range of duties; however, the RO should demonstrate a consistent pattern of constant engagement through effective avenues of communication with which the RO has delegated this authority. The RO must, however, retain final decision-making responsibility over matters concerning overall programmatic compliance with the select agent regulations. In other words, the RO may delegate day-to-day maintenance activities or decisions to an ARO but may not delegate those decisions that affect the nature or complexity of an entity's select agent program.

Security Risk Assessment

The regulations in Section 9(a)(1) require that the individual designated to be the RO must have a SRA. A SRA renewal is required once every three years. While each RO is notified by the FSAP prior to expiration of the SRA, it remains the RO's responsibility to ensure that his or her SRA renewal is submitted in time to avoid expiration.

All individuals who have access to select agents and toxins are required to obtain a SRA prior to such access and to undergo a renewal of their SRA every three years. Individuals with select agent and toxin access must submit a new completed Form FD-961 to CJIS at least 45 days prior to the three year expiration date. Please note that finger prints are not normally required for renewals unless specifically requested by CJIS. The FSAP assists in this process by providing the RO with the names of individuals due for renewal of their SRA approximately 90 days in advance of the SRA expiration. If CJIS does not receive the required information from the individual prior to expiration or with insufficient time to process the Form FD-961 the individual's access to select agents and toxins must be terminated by the RO. If at any point an individual's access to select agents and toxins is terminated the RO is expected to immediately report this to the FSAP with a statement of the reason for the termination. The RO is required to discuss the SRA process with each individual required to have access to and sign the individual's FD-961 before sending to CJIS. Additional information on the SRA process can be found in Chapter 7. The FSAP recognizes that the termination of access to select agents and toxins when an entity will begin actions to remove an individual from its registration, is different than when an entity temporarily suspends access due to authorized absences. The entity is not required to report to the FSAP temporary

suspensions of access; however, if this removal does become permanent, then the FSAP must be notified.

Knowledge of the Select Agent Regulations

Section 9(a)(2) of the Select Agent Regulations specifies that the RO is required to be familiar with the requirements of the select agent regulations. The select agent regulations also state that the RO is responsible to ensure that the registered entity is in compliance with all the requirements of the select agent regulations (See section 9(a)(4)) This means that the RO is responsible for the security, biocontainment and safe use of BSAT agents and toxins at his or her entity. Since the RO certifies the information on all APHIS/CDC Forms 1 through 4 is, to the best of his or her knowledge, accurate and truthful, it is imperative that the RO become familiar with and fully understand the Select Agent Regulations and make him or herself aware of associated FSAP policy and guidance documents that are available to assist in the implementation of a successful program. The RO should have sufficient understanding of the work objectives within their BSAT operations in order to make appropriate management decisions regarding security, biocontainment and biosafety, and incident response.

In addition to the Select Agent Regulations, there are FSAP policies and guidance posted on the Select Agent Program website. The guidance documents have also been included in the Appendix of this manual. The FSAP develops guidance documents to help clarify the intent of the regulations and the policies of the FSAP in implementing these requirements. Under most circumstances, the RO will be notified by electronic mail (e-mail) of new developments or documents posted on the website. These are called "SAGrams". The intent of this manual is to provide a resource for the RO that collects the information resources available to the RO in one location.

A FSAP file manager is assigned to each entity to serve as an additional resource for information and assistance. The file manager handles all registration issues, incoming requests for amendments, inspection information, and compliance issues of their assigned registered entities. In addition, the FSAP employs security, facility, incident response, occupational health and biosafety experts which are available to advise RO's. The assigned file manager can assist in making these resources available to the RO.

Periodically, the FSAP will conduct workshops or webinars specifically targeted to the regulated community. The purpose of these events is to keep the regulated community current about upcoming changes, and to respond to entity questions. The RO will be notified when these events are available through e-mails, public notification and the NSAR website.

Authority and Responsibility

Section 9(a) (3) of the Select Agent Regulations requires that the RO has authority and responsibility to act on behalf of the entity. As noted earlier, the RO certifies all the information submitted to the FSAP on APHIS/CDC Forms 1, 2, 3, and 4 is, to the best of his or her knowledge, accurate and truthful. The entity must have delegated to the RO the authority to effectively manage the biosecurity, biocontainment and biosafety, and incident response of BSAT in their facility. The RO must have the ability to provide direct input to affect changes as needed in operations, personnel, and facilities at the registered entity in order to fulfill his or her responsibilities. The RO position must be such that employees engaged in BSAT activities at the entity recognize the RO's authority to maintain compliance with the select agent regulations. The RO must have the ability and opportunity to effectively communicate with senior management within the entity in order to gain support and obtain actions as needed in carrying out his or her responsibilities. For example, the RO should

have the ability to either make budget decisions or influence these decisions to ensure that necessary actions are taken for equipment maintenance, repairs of the biocontainment facilities, and physical security systems used to protect and secure BSAT in compliance with the select agent regulations.

While the RO can delegate duties to others to achieve efficiencies in oversight; the RO retains responsibility to ensure that the registered entity is in full compliance with the select agent regulations. Accordingly, the RO should maintain constant engagement with those to whom he or she has delegated duties. For example, while the RO can delegate to an ARO or other subordinate oversight of the biosafety plan and biosafety issues in the entity's BSAT program, the RO should be aware of the overall biosafety concerns of BSATs at the entity and any ongoing issues through regular briefings by those to whom tasks have been delegated. The select agent regulations require that an ARO have the appropriate knowledge, competence, and authority to execute the full duties of the RO in the RO's absence. The ARO must have the sufficient capability and authority to perform all duties of the RO.

It should also be noted that an ARO is not an "assistant" RO and should only conduct functions as the RO while the RO is offsite. The ARO must have the ability to assume the full authority and undertake all of the responsibilities of the RO as needed. While the RO may delegate certain functions to others, including the ARO, the RO must retain his or her overall responsibility for oversight of the delegated functions. The RO must retain oversight of the decisions that would necessitate changes to the registration and submission of documents to the FSAP, but the ARO can sign documents and submit forms and information in support of those decisions. It is important that the RO maintain control over all aspects of an entity's program and be aware and responsible for all submissions to the FSAP. The RO should be fully engaged in his or her duties when on site, but can delegate administrative and maintenance functions of the entity's select agent program as necessary to ensure the efficiency and timeliness of communications with the FSAP.

The RO, in order to ensure effective compliance with the Select Agent Regulations, should either be in charge of, or involved with, certain supervisory or management functions of employees with access to BSAT at the registered entity. The scope of responsibilities includes limiting access to BSAT to SRA approved personnel, initial and refresher training, and performance oversight and disciplinary action of employees engaged in work with BSAT. The FSAP has found that ROs who are knowledgeable about, and interact with, individuals approved to work with BSAT, are more successful in carrying out their responsibilities.

While specific roles (e.g., fulfilling the responsibilities of an absent RO) may be fulfilled only by an approved ARO, other duties may be delegated to other individuals at the entity. Delegated duties may include developing risk assessments; developing written security, incident response and biosafety plans; training select agent personnel; developing and maintaining safety, security, or incident response protocols; maintaining BSAT records; and submitting APHIS/CDC Forms approved by the RO. Despite these delegations of authority, the RO is still responsible for maintaining current knowledge of what is occurring within his or her entity.

With respect to the granting of access to select agents and toxins, the registered entity retains the authority to make decisions concerning access even if an individual has been approved by the FSAP to have access to select agents and toxins. We note that the first step in granting approval to have access to select agents and toxins is the identification by the entity of an individual that the entity wishes to have access to the select agents and toxins that it possesses. Regardless of whether there is sufficient cause to terminate an employee's employment at an entity, the RO should have the authority to

terminate an individual's access to select agents and toxins at any point based on knowledge that this individual poses a security or safety risk of any sort, seriousness, or magnitude.

Compliance with the Select Agent Regulations

The following are specific items and duties which are required and are the responsibility of the RO to maintain compliance with the select agent regulations:

Security, Biosafety and Incident Response Plans:

- Create and maintain a site-specific, security plan designed according to a site- specific risk assessment that provides graded protection in accordance with the risk of the select agents and toxins for which the entity is registered.
- Create and maintain an agent-specific, site-specific biosafety plan commensurate with the risk of the select agents and toxins, and its use, for which the entity is registered that contains sufficient information and documentation to describe biosafety and containment procedures.
- Create and maintain a site-specific incident response plan commensurate with the hazards of the select agents and toxins for which the entity is registered that fully describes the entity's response procedures for the theft, loss, or release of a select agent and toxin, inventory discrepancies, security breaches, natural disasters and other emergencies.
- Review the security, biosafety and incident response plans annually and revise them as necessary, including after any drill or exercise, and after any incident.
- Conduct site-specific drills or exercises at least annually to validate or test the effectiveness of the security, biosafety and incident response plans.
- Provide information and training on incident response, biosafety and security to each individual with access approval prior to him or her having access to select agents and toxins; with refresher training provided annually. This training must be documented.
- Provide situation appropriate training to individuals escorted into registered space on incident response, biosafety and security prior to entering into registered space. This training must be documented.
- Ensure coordination and communication with the entity biosafety and security officials to assess potential personnel security issues.
- Review and maintain the entity's pre-access and on-going suitability assessments for individuals with access to Tier 1 agents.
- Ensure the entity has an active insider threat awareness training program, especially for entities possessing Tier 1 agents.
- Conduct and document annual inspections for each laboratory and storage area (all registered spaces) where select agents and toxins are stored or used.

Records:

Maintain all records related to the registration and approval to possess, use, and/or transfer select agents and toxins as required by the select agent regulations for at least 3 years to include:

- an accurate, current inventory for each select agent and toxin held in long term storage,
- information about all entries into areas containing select agents and toxins, and
- a current list of all individuals that have been granted select agents and toxins access approval.

FSAP Notification:

- Submit an amendment for any change in circumstances to the certificate of registration, including, but not limited to:
  - adding or removing individuals,
  - the addition of laboratory or storage area(s) prior to use or storage of select agents and toxins in the area,
  - any changes to RO or ARO contact information, or
  - changes to registration such as addition or deletion of select agents and toxins and animal species and areas.
- Submit an amendment describing work prior to conducting a restricted experiment as defined in Section 13.
- Ensure personnel who will have access to Tier 1 select agents and toxins are enrolled in a pre-access assessment.
- Ensure ongoing suitability monitoring of personnel with access to Tier 1 select agents and toxins.
- Request approval (APHIS/CDC Form 2) prior to inter-entity transfer of a select agent and toxin, with exceptions defined in Section 16.
- Upon discovery of a theft or loss of a select agents and toxins, immediately notify the FSAP and appropriate Federal, State, or local law enforcement agencies. An APHIS/CDC Form 3 must be submitted within seven calendar days upon discovery of a theft or loss.
- Upon discovery of a release of a select agent and toxin causing occupational exposure or release of a select agent and toxin outside the primary barriers of its biocontainment area, immediately notify the FSAP. An APHIS/CDC Form 3 must be submitted within seven calendar days upon discovery of a release.
- Immediately report the identification of any Tier 1 select agents and toxins to the FSAP and other appropriate authorities when required by Federal, State, or local law.
- Submit APHIS/CDC Form 4 for:
  - the identification and final disposition of a select agent and toxin contained in a specimen within seven calendar days of identification, and
  - the final disposition of any select agents and toxins contained in a specimen presented for proficiency testing within 90 calendar days of receipt of the sample.

Internal Inspections of Laboratories

Section 9(a) (6) of the Select Agent Regulations requires the RO to ensure that annual inspections are conducted for each laboratory where BSATs are stored or used in order to determine compliance with the requirements of the select agent regulations. Establishing an internal annual inspection program provides a means for the RO to monitor compliance with the Select Agent Regulations and identify deviations from acceptable laboratory safety practices. An established schedule for recertification and service of laboratory equipment (e.g., biosafety cabinets, HEPA filters and rendering units) will also help identify any potential gaps in biocontainment. Internal unannounced inspections of laboratory space during ongoing research projects can help identify any deviations from established biosafety, or security standard operating procedures. The annual inspection should also include a review of the entity's BSAT inventory procedures to ensure that individuals with access to BSAT inventories are following appropriate procedures for access and recording changes to the inventory. This can be separate from an overall periodic reconciliation

of the entire inventory (recommended every year). The annual check does not have to be all inclusive but can be done through spot checks of the inventory to ensure that appropriate procedures are being followed for changes, access, and security of the inventory. Annual reviews of the biosafety plan, security plan, and incident response plans are required and ensure that any changes in the facility operations are appropriately captured. These annual reviews should be appropriately documented, with names, dates, and findings noted for review by the FSAP upon request.

Principal Duty Station

Section 9(a)(5) of the Select Agent Regulations requires the RO have a physical (and not merely a telephonic or audio/visual) presence at the registered entity to ensure that the entity is in compliance with the select agent regulations and be able to quickly respond to on-site incidents involving BSAT. Ideally, the RO should be co-located with the entity, or within reasonable distance of the entity's registered facilities, to be able to quickly respond to emergencies and to provide appropriate oversight on a day-to-day basis. Based on ten years of experience the FSAP believes that effective oversight and control cannot be properly achieved by an RO located at some distant location. There must be an approved RO, or ARO when the RO is absent, at a registered entity during normal business hours and the RO, or ARO, must be available for emergencies after normal business hours. The FSAP recognizes there are situations where registered entities have two or more registered laboratory facilities dispersed over a defined geographical location (e.g., a university campus or business complex). The FSAP considers this one general physical location which can be managed under one registration provided the entity has a single official street address. The intent of the requirement that the RO have a physical presence at the registered entity is not to require that an RO be assigned to each laboratory but to ensure that an RO is physically located on-site. The RO should have the responsibility, as discussed in this document, over the entire registered entity, even if the registered entity contains multiple buildings.

The Responsible Official Guidance Document provides additional information on duties and responsibilities.

Chapter 2 Quiz

CHAPTER 3: REGISTRATION WITH THE FSAP – APPLICATIONS AND AMENDMENTS

OBJECTIVE: To become familiar with the requirements for registering with the Federal Select Agent Program (FSAP) and the process of submitting amendments when there are changes to the entity registration.

For self-study it is recommended that you take the Self-Evaluation Exam after you have completed reading the chapter. Compare your answers with the answers provided to identify any areas for additional study.

If you are an unregistered entity you will not have been assigned a file manager but if you contact the FSAP and ask for the Operations Branch Manager or an Operations Team Lead you will receive assistance. The FSAP-assigned file manager can assist you with any problems in completing an application and submitting amendments. The APHIS/CDC Form 1 contains the registration form and specific instructions on how to complete it.

Deciding to Apply for Registration

An entity cannot legally possess, use or transfer select agents and toxins if they are not registered with the FSAP. In deciding whether to register the entity the following should be considered:

- What kinds of biological agents and toxins (BSAT) does the entity want to possess, and are they agents and toxins that require registration with FSAP? Some biological organisms and toxins have been excluded from the requirements of the select agent regulations. Select Agents and Toxins List contains the list of select agents and toxins.

- If toxins are to be possessed, will amounts under the control of a principal investigator, treating physician, veterinarian, commercial manufacturer or distributor exceed at any time the limit required for registration? Select Agent and Toxin Exclusions provide the quantity amount on toxin limits. If the level of toxins possessed by the entity will never exceed the limit requiring registration, there is no requirement to be registered. Please note that there is the "toxin due diligence" provision requires a person transferring toxins in amounts which would otherwise be excluded from the provisions to: (1) use due diligence to assure that the recipient has a legitimate need to handle or use such toxins; and (2) report to Federal Select Agent Program if they detect a known or suspected violation of Federal law or become aware of suspicious activity related to the toxin.

- What work will be performed with the select agents and toxins? If the entity will be conducting research with toxins above the limit required for registration or if the laboratory will be using select agents and toxins for quality control of diagnostic tests registration is required. If the laboratory will be receiving specimens or samples for diagnosis, or as part of a proficiency program, and will not maintain select agents or toxins, there may not be a need to submit an application.

- Does the entity have the containment facilities and support systems required for work with the agents and toxins they wish to possess?

- Is the entity performing work with Tier 1 select agents? Select Agents and Toxins List contains the list of Tier 1 agents.

- Is there top level management support for an entity select agent program?

- Does the entity have the resources necessary

to meet the requirements of the Select Agent Regulations? The Quick Reference at the beginning of this manual is intended to provide an overview of the requirements.

Preparation for the Registration Process

If an entity decides to possess, use, and transfer, select agents and toxins there are some additional questions and activities to consider before beginning the application process. They are the following:

- Will animals be used? If animals are to be used, what kind? The requirements for small animals are different from large animals. There are animal care and use requirements that the entity should be aware of. These are not requirements of the Select Agent Regulations but they may impact how the entity structures the biosafety program and uses select agents and toxins.

- Will arthropods be used? Will plants be used? These require special facilities. Do they exist at the entity or will they need to be constructed?

- What biosafety level is required for the type of agent and the work to be performed? *Biosafety in Microbiological and Biomedical Laboratories* for the recommended biosafety levels for the various select agents and toxins. Keep in mind that the volume of agent and the way the agent is used are factors that should be considered in the biosafety level required.

- Do laboratories located within the entity meet the required biosafety level and are they fully operational or ready to go operational? If not, what is the estimated time when they will become operational? If laboratory construction has not been started, or has begun but is not complete, the entity should delay submitting an application until construction is compete and the laboratory is ready to begin operations. Contact the FSAP if you have questions about when to submit an application. The FSAP will conduct an on-site inspection of all laboratories to be registered and any laboratory to be registered should be capable of full operations at the time of inspection.

- If the laboratory is a BSL-3/ABSL-3 or BSL-4/ABSL-4, has the laboratory been commissioned? There is more information on laboratory commissioning in Chapter 14. If the laboratory has not been commissioned it is better to hold off on submitting the application until the commissioning is completed or is close to completion.

- Review Chapter 2 on responsibilities of the Responsible Official (RO) and decide who in the organization is most suitable to serve in this capacity. Where does this person sit in the organization and what kind of authority will the person have in the organization for matters related to BSAT?

- Become familiar with the regulations that apply to the entity and review those parts of the Biosafety in Microbiological and Biomedical Laboratories (BMBL), 5th Edition that applies to the agents that will be used.

- Make sure you have engaged everyone in your organization that will work with BSAT or will be supporting the BSAT work. This may be researchers, laboratory managers, information technology management, entity senior management, facility engineers, security, and animal care personnel.

- Ask a member of the FSAP questions you have about the registration process, send inquiries to either lrsat@cdc.gov or AgSAS@aphis.usda.gov.

Preparing the Application

If the organization has determined that the work they are planning to conduct will require the possession, use and transfer of BSAT, and they have

decided to begin the registration process, the next step is to identify a RO, if that has not been done already. The RO is the point of contact through which the FSAP communicates with the entity. This requirement helps to facilitate the communication between the FSAP and the entity and to avoid miscommunication issues. The RO does not need to have a FBI Security Risk Assessment (SRA) at this point but must have one before the entity can be registered.

The registration process begins by completing the *Application for Registration for Possession, Use and Transfer of Select Agents and Toxins* (APHIS/CDC Form1). The *Guidance Document for the Completion of APHIS/CDC Form 1* provides step-by-step instructions on how to complete the form. In large entities, the RO may find it helpful to delegate the task of providing the information requested on the forms and then compiling the information into one package to send to FSAP. The FSAP should be contacted if any problem is encountered in accessing the form.

Submitting the Application

After the application is completed, the application should be sent to either the Agriculture Select Agent Program (AgSAS) at the Animal and Plant Health Inspection Services (APHIS) or the Division of Select Agents and Toxins (DSAT) at the Centers for Disease Control and Prevention (CDC). The AgSAS and the DSAT operate the FSAP but for administrative reasons entity applications are processed by one or the other. To determine where to send the application the RO should consider the following:

- If the select agents and toxins that the entity wishes to register for are HHS Only agents and toxins the entity should send the application to the DSAT.
- If the select agents and toxins are USDA only (animal or plant agents) the application should be sent to AgSAS.
- If the select agents and toxins are Overlap or both HHS and animal or plant agents the application can be sent to either AgSAS or DSAT.

To determine which agents and toxins are HHS only (human), USDA only (animal and plant) and overlap please refer to the Select Agents and Toxins List. If you are uncertain where to send the application, contact the DSAT or AgSAS for assistance.

Processing the Application

After the FSAP receives the application from the entity, it is assigned to a file manager. This is the point of contact at the FSAP, and the person who the RO should communicate with on all select agent matters. This relationship is a very important because the file manager works closely with the RO to ensure that the FSAP is kept up to date on changes at the entity and to respond to questions the RO has about the requirements.

In response to the submission of the APHIS/CDC Form 1, the RO will receive a letter from the FSAP containing unique Department of Justice (DOJ) numbers for each of the individuals that have been identified by the entity on the APHIS/CDC Form 1. The RO provides the assigned DOJ number to each individual who submits a security risk assessment (SRA). Please note that the RO must discuss the application with the individual and cosign the form before it is sent to CJIS.

While the SRA request is being processed the RO should begin preparation for the onsite inspection which is described in detail in Chapter 13. An inspection is required before registration of the entity and this inspection normally will occur within 60 – 90 calendar days after the application is submitted.

Registration

Upon completion of the inspection process and the submission of an approved APHIS/CDC Form 1, a registration Certificate will be issued. This normally occurs within 90 – 120 calendar days from the date the application is submitted. Failure to provide adequate information, delays in responding to requests for information, failure to respond to inspection-noted deficiencies, or incomplete facilities are circumstances that can delay registration. The entity registration is valid for a period of up to three years unless the registration is suspended or revoked due to the entity's failure to be in compliance with the regulatory requirements.

Amending the Entity Registration

Anytime there is a change at the entity the RO must provide an amendment to the registration by submitting the appropriate sections of the APHIS/CDC Form 1 to the FSAP. Examples of changes that require an amendment include the following:

- The entity wishes to add a new agent or toxin to the registration or to remove an agent or toxin.
- A person is hired by the entity who needs a security risk assessment (SRA) or a person resigns and must be removed from the list of individuals with access.
- A new laboratory is added or a laboratory is no longer used for select agents and toxins.
- A new project is planned that involves work not previously described (e.g., work with different species of animal).
- The RO, a PI, or ARO, is planning to leave the entity.

There are instructions on submitting amendments. When the amendment is submitted a letter acknowledging the receipt of the amendment is sent to the RO by the FSAP. The amendment is reviewed by the file manager, and the file manager contacts the RO for any additional information that may be required. In some cases, such as the addition of laboratories, new agents or new work objectives, an onsite inspection may be required. If the entity is registered with the CDC and the entity is adding USDA only agents the USDA must concur on the approval of the amendment. If the entity is registered with the USDA and HHS only agents are being added the CDC must concur. Most amendments can be processed in less than two months but amendments that require concurrence or an onsite inspection may take longer.

Chapter 3 Quiz

CHAPTER 4: REPORTING REQUIREMENTS

OBJECTIVE: Become familiar with the types of reports that must be submitted to the FSAP, the circumstances under which reports must be submitted and deadlines for reporting.

For self-study it is recommended that you take the Self-Evaluation Exam after you have completed reading the chapter. Compare your answers with the answers provided and review any areas were you did not provide the correct answers. Please contact the FSAP if there are questions about the content of this chapter or you have questions not answered by the information provided.

APHIS/CDC Form 4, APHIS/CDC Form 3 and guidance on completing these forms are available. As a matter of general interest an article was published in the Applied Biosafety, Vol. 17, No. 4, 2012, *Monitoring Select Agent Theft, Loss and Release Reports in the United States – 2004 – 2010*, which describes the reports received by the FSAP over a six year period.

Introduction

There is a requirement to notify the FSAP of the theft, loss or release of a select agent or toxin (APHIS/CDC Form 3), and an identification of a select agent and toxin (APHIS/CDC Form 4). Institutions that only conduct research will not likely have any occasion to use the APHIS/CDC Form 4. Entities conducting diagnostic testing however will find that they will utilize the APHIS/CDC Form 4 extensively. The requirements for reporting a theft, loss or release are found in Section 19 of the select agent regulations (42 CFR §73.19, 9 CFR §121.19 and 7 CFR §331.19) and the requirements for reporting a confirmed select agent and toxin is found in sections 3, 4, 5, 6 and 9 of the regulations.

Reporting of the Identification of Select Agents and Toxins

Any clinical or diagnostic laboratory, whether registered with the FSAP or not, is required to report any select agents and toxins they identify. It is important to note that only those agents and toxins that are confirmed to be a select agent or toxin are required to be reported. It is not necessary to report a select agent or toxin for which there is only presumptive evidence, however, it is prudent for the laboratory to ensure that the agent or toxin is maintained securely until a confirmation test is performed to verify if it is a select agent or toxin.

If the select agent or toxin has been isolated from a clinical specimen or environmental sample it must be reported to the FSAP using APHIS/CDC Form 4A. Along with this form, there is a list of frequently asked questions and guidance for completing the form. There is also a reporting requirement if the laboratory has identified a select agent or toxin from a proficiency sample. The APHIS/CDC Form 4B is used for reporting proficiency samples as well.

Immediate Notification

There are specific deadlines for reporting the identification of a select agent and toxin and it is important to observe these. The select agents and toxins listed below must be reported immediately to APHIS/AgSAS or CDC/DSAT via telephone, fax or e-mail and the APHIS/CDC Form 4 submitted within 7 days after identification.

- *Bacillus anthracis*
- Botulinum neurotoxins
- Botulinum neurotoxin producing species of Clostridium
- *Burkholderia mallei*
- *Burkholderia pseudomallei*

- Ebola virus
- Foot-and-mouth disease virus
- *Francisella tularensis*
- Marburg virus
- Rinderpest virus
- Variola major virus (Smallpox virus)
- Variola minor virus (Alastrim)
- *Yersinia pestis*

All other agents and toxins not listed above are not required to be reported immediately but they must be reported within 7 days using APHIS/CDC Form 4A to the FSAP.

If the select agent or toxin is isolated and identified from proficiency sample the entity has 90 days from the date receipt to report to the FSAP using APHIS/CDC Form 4B.

Disposition of Agents

There are also requirements for disposition of the identified select agents and toxins and they are as follows:

- If the entity is registered for the select agent or toxin it may transfer, retain or destroy the agent or toxin. The entity may retain the select agent or toxin for as long as they are registered for the select agent or toxin.

- If the entity is registered with the FSAP but is not registered for the select agent or toxin that has been identified they must transfer or destroy the select agent or toxin within 7 days of identification.

- If the entity is not registered with the FSAP they must destroy or transfer the select agent or toxin within 7 days of identification.

- A clinical or diagnostic laboratory must report the identification of any select agent toxin regardless of the amount.

If the entity wishes to transfer the select agent or toxin rather than destroy it because they believe it may have some scientific value contact the FSAP who may be able to assist in identifying the name of entities who can receive the agent or toxin.

If the entity wishes to transfer the select agent or toxin to an entity that is registered for the select agent and toxin they must first obtain approval to transfer the select agent or toxin by completing APHIS/CDC Form 2 – Request to Transfer of Select Agents or Toxins and sending the request to the FSAP.

Reporting a Theft, Loss or Release of Select Agents and Toxins

The requirements for reporting a theft, loss or release are found in section 19 of the Select Agent Regulations (42 CFR §73.19, 9 CFR §121.19 and 7 CFR §331.19).

A theft is the unauthorized removal of a select agent or toxin from an individual or entity to whom it is registered or from a location where the select agent or toxin is approved to temporally exist such as with a courier or at a diagnostic laboratory. A loss is the situation where a select agent or toxin cannot be found or accounted for which was previously known to exist. A release is either an occupational exposure or an event that results in the discharge of a select agent or toxin outside the primary containment barrier. The event can be the result of a spill of infectious material or a failure of the containment system. Any incident that results in the activation of a post exposure medical surveillance/prophylaxis protocol should be reported as a release. Laboratory acquired infections are often not associated with an apparent occupational exposure.

The first action taken by the FSAP upon notification of a theft, loss or release report is to collect information necessary to determine if there is a potential threat to the public health (humans, animals or domestic plants) posed by the incident.

Thefts or loss of BSAT in transit or a release outside the secondary biocontainment barrier of a laboratory are examples of incidents that may pose significant public health concerns and may require immediate action by emergency responders and law enforcement.

The RO is responsible for ensuring that any time there is a theft, loss or release of a select agent or toxin that this is immediately reported to the FSAP. This should be followed by submitting an APHIS/CDC Form 3 within 7 days of the incident. Reporting should be done by telephone, facsimile or e-mail. Facsimile or e-mail notification is recommended as it provides the entity with documentation of the report. If the entity is registered with the APHIS/AgSAS use the following address for immediate notification and for submitting the Form 3.

Animal and Plant Health Inspection Services (APHIS)
Agriculture Select Agent Services
4700 River Road Unit 2, Mailstop 22, Cubicle 1A07
Riverdale, MD 20737
Tel: 301-851-3300 (Option 3)
Fax: 301-734-3652
E-mail: AgSAS@aphis.usda.gov

For those entities that are registered with the CDC/DSAT the reporting should be to the following:

Centers for Disease Control and Prevention
Division of Select Agents and Toxins
1600 Clifton Road NE, Mailstop A-46
Atlanta, GA 30333
Tel: 404-718-2000
Fax: 404-718-2096
E-mail: form3@cdc.gov

If uncertain about who the entity is registered with either address is acceptable or an e-mail can be sent to LRSAT@cdc.gov.

Anytime there is a theft, loss or release at the entity, or during the transit of select agents and toxins to or from the entity, it is critical that the RO, in addition to reporting the incident, immediately collect as much information on the circumstances surrounding the event as possible, ensure that any individual exposed, or potentially exposed, is provided access to health care givers and cease operations and/or secure the area as appropriate. The RO and other members of the entity should also be prepared to provide assistance to local, state and federal agencies as they require.

Reporting Theft or Loss

The information the RO should collect in the event of a theft or loss is the following:

- The name of the select agent or toxin and any specific identifying information such as strain or genetic profile
- An estimate of the quality lost or stolen either as vials or in the case of toxin volume
- The date and time that the loss, or theft, was discovered and an approximation of when the theft or loss is suspected as occurring.
- The location, building, and room, from which the loss or theft occurred.
- A list of local, state and Federal agencies notified or that will be notified.
- Any other details pertinent to the incident.
- Actions taken to assess the reasons for the theft taken to correct any operational issues to address the reasons.

Reporting Release

The information the RO should collect in the event of a release is the following:

- The name of the select agent or toxin and any specific identifying information such as strain or genetic profile.

- An estimate of the quantity released.
- The time and duration of the release
- The environment into which the release occurred
- Number of individuals potentially exposed
- Actions taken to respond to the release
- Hazards posed by the release
- Any other details pertinent to the incident
- Actions taken to prevent future reoccurrences

The RO should be aware, should they be asked, that there is a requirement for non-registered laboratories which experience a theft, loss or release incident of a confirmed select agent or toxin to report this to the FSAP using the contact information provided above.

The RO must also contact local, state or federal law enforcement agencies of any theft or loss of select agents and toxins and should notify local, state or federal health or agriculture agencies if there is a release. These procedures should be described in the entity incident response plan or in a standard operating procedure that is referenced in the entity incident response plan.

When there is a report of a theft, loss or release by an entity the FSAP will normally contact the entity to request additional information. In some circumstances the FSAP will conduct an onsite inspection of the entity to collect additional information and to advise the entity on possible procedure corrections. In the event of a theft the entity may also be contacted by the Federal Bureau of Investigation (FBI).

A copy of APHIS/CDC Form 3, instructions for completing the form and additional information to assist the RO to define a theft, loss or release of select agents or toxins is available.

Retention of Records

APHIS/CDC Form 3, Report of Thief, Loss and Release and APHIS/CDC Form 4, Report of Identification of Select Agents and Toxins must be maintained securely for a minimum of three years after the report. The RO may be asked during an onsite FSAP inspection to produce these records.

Chapter 4 Quiz

CHAPTER 5: TRANSFERS OF SELECT AGENTS AND TOXINS

OBJECTIVE: To be able to complete a request to transfer select agents and toxins, be familiar with the requirements for transferring select agents and toxins and be familiar with the requirements after transfer and how to respond if there is a problem with the transfer.

For self-study it is recommended that you take the Self-Evaluation Exam after you have completed reading the chapter. Compare your answers with the answers provided and review any areas where you did not provide the correct answers. If you have questions about the information provided or you have questions that are not covered by the material in this chapter contact the FSAP for assistance.

APHIS/CDC Form 2 and the guidance document to complete the form are available. The forms and instructions change occasionally and it is important to ensure you are using the most current form.

Introduction

The requirements for transferring select agents and toxins from one entity to another are covered in Section 16 of the Select Agent Regulations (42 CFR §73.16, 9 CFR §121.16, 7 CFR §331.16). Select agents and toxins can only be transferred upon approval by the FSAP. Diagnostic laboratories that are not registered can transfer select agents and toxins to registered laboratories but they must obtain approval prior to the transfer.

Conditions for Authorization of Transfer

Authorization for transfer may be provided under the following circumstances:

- The sender and the receiver of the select agent and toxin are both registered for the select agent or toxin. For example, Entity A, who is registered for *B. anthracis* cannot transfer *B. anthracis* to Entity B if Entity B is not registered to possess *B. anthracis* but can transfer *B. anthracis* to Entity C who is registered for the agent.

- If the sender of the select agent or toxin is exempted from the regulations, a diagnostic laboratory for example, the laboratory can receive authorization to transfer the agent or toxin to a laboratory that is registered to possess the agent or toxin. It is important to note that a laboratory must receive authorization to transfer the select agent or toxin before doing so. However, the laboratory that is exempt from the regulations does not need authorization to transfer the agents or toxins if it has not been confirmed that the agent or toxin is a select agent.

- If the select agent or toxin is imported from outside the United States the transfer may be approved even though the sender is not registered providing that the recipient is registered for the agent.

Proficiency Samples/Specimens

The regulations permit the sender to transfer samples or specimens for proficiency testing without completing the APHIS/CDC Form 2 providing that the FSAP has been notified at least seven calendar days prior to the transfer of the select agents and toxins and the FSAP is notified as to which agents and toxins will be sent and to whom they will be sent. The recipient would complete APHIS/CDC Form 4B reporting the identification of a select agent or toxin.

Special Circumstances

The regulations allow the HHS Secretary or APHIS Administrator to authorize transfers of select

agents and toxins which would not otherwise be authorized under conditions determined by the HHS Secretary and/or APHIS Administrator. These decisions are made on a case by case basis. A possible situation where this might apply is an outbreak of disease caused by a select agent virus that requires the services of laboratories not registered for the virus.

Laboratories whose registrations have been suspended or have agreed to maintain their agents and toxins in storage only because of regulatory deficiencies are not generally authorized to conduct transfers until the entity has resolved the deficiencies.

Entities that transfer toxins below the limit requiring registration are not required to obtain approval to transfer the toxin, however they must only transfer the toxin after conducting due diligence and documentation that the recipient has a legitimate need to use and possess the toxin. They must also report to the CDC/DSAT if they detect a known or suspected violation of Federal law or become aware of suspicious activity related to toxins.

Authorization to transfer select agents and toxins within a registered entity does not require approval from the Federal Select Agent Program. An example is the transfer of select agents from one registered principal investigator to another registered principal investigator in the same institution; an intra-entity transfer. While submission of an APHIS/CDC Form 2 to the FSAP is not required for intra-entity transfers, it is important for the RO to establish procedures for documenting these transfers and to ensure that safe and secure requirements are met. The regulatory requirement that specifies this is in section 11 of the Select Agent Regulations (73.11(d)(5) 121.11(d)(5), 331.11(d)(5)) which states, "(d) An individual or entity must adhere to the following security requirements or implement measures to achieve an equivalent or greater level of security: (5) Establish a protocol for intra-entity transfers under the supervision of an individual with access approval from the Director, DSAT or the Director, AgSAS including, chain-of-custody documents and provisions for safeguarding against theft, loss or release,".

An entity may find it necessary due to an emergency situation to transfer storage of select agents and toxins from a registered space within the entity to an unregistered space within the entity. If this occurs the RO must immediately notify the FSAP and must ensure that the select agents and toxins are secured to prevent unauthorized access. If circumstances permit, the RO should notify the FSAP before the move of the select agents and toxins.

Procedures for Transfer Approval

The procedures for obtaining approval to ship and receive select agents and toxins, a copy of APHIS/CDC Form 2 and instructions for completing the form, and a list of frequently asked questions is provided at FSAP website. This information will not be duplicated in this chapter but it is recommended the RO acquire an understanding of the process before shipping or receiving select agents and toxins. The RO should also contact the FSAP if they have any questions.

Authorization for transfer is valid for a period of 30 calendar days. If the intended recipient does not receive the select agents and toxins within 48 hours after shipment, or if the package appears to be damaged, or to have been tampered with, or the agents and toxins received are not what was authorized to be shipped the RO must immediately notify the FSAP by telephone, fax or e-mail.

Security and the Transfer of Select Agents and Toxins

The regulatory requirements for entity security are covered in Chapter 7 however it is appropriate to discuss security of select agents and toxins in the context of transfers since it encompasses additional

consideration beyond the entity security.

Section 11(c)(10) of the Select Agent Regulations states that the entity security plan must "Contain provisions and policies for shipping, receiving, and storage of select agents and toxins, including documented procedures for receiving, monitoring, and shipping of all select agents and toxins. These procedures must ensure that an entity will properly secure select agents and toxins on-site and have a written contingency plan for unexpected shipments". Responsible Officials should work with all staff involved (i. e. principle investigators, laboratory staff, shipping/receiving, and security) to ensure that all outgoing and incoming shipments are handled in accordance with the regulations and that protocols are in use to handle unexpected events during shipping and receipt. Training on the protocols should also be conducted.

The transportation of hazardous materials, including select agents and toxins, which are transported over public transport routes is governed by the U.S. Department of Transportation's Hazardous Material regulations found in Title 49 of the Code of Federal Regulations, Parts 100-185. Transportation in commerce starts when a select agent or toxin has been packaged for shipment and is ready for receipt by a courier or commercial carrier. It ends when the package is received by the intended recipient who must be an individual approved by the Director, DSAT or Director AgSAS to have access to select agents and toxins.

In a May 2009 report published by the Defense Science Board Task Force on Department of Defense (DOD) Biological Safety and Security Program, the Task Force recommended that the "lost in the crowd" approach be used for all shipments of biological select agents and toxins involving DOD labs. In addition, the Department of Transportation (DOT) has performed over 100 inspections of entities transferring select agents and toxins to ensure that these entities are complying with DOT regulations. The Federal Select Agent Program, in collaboration with DOT, has developed guidance for the regulated community on the shipping and packaging of select agents. This guidance includes information on all applicable domestic and international shipping regulations.

The Federal Select Agent Program has amended the select agent regulations so regulated entities that maintain shipping and receiving facilities in compliance with DOT hazardous substance regulations, and have procedures that are able to maintain select agent and toxin anonymity in shipping/receiving facilities, (i.e., preserving "lost in the crowd"), will not be required to register these areas even if packages not identified as containing select agents or toxins, will temporarily be stored in these areas. For entities preserving the "lost in the crowd" concept during shipping and receiving, the select agent regulatory oversight for recipients begins when a select agent package arrives at its ultimate destination for unpacking by an individual approved for access by the Director, DSAT or Director, AgSAS. Select agent oversight for senders covers all use of the regulated materials up to the time that the materials are packed for shipment, in compliance with DOT hazardous materials regulations, by an individual approved by access by the Director, DSAT or Director, AgSAS.

Packaging for shipment

The packaging of a select agent or toxin must be performed by an individual approved by the Director, DSAT or Director, AgSAS for access to select agents and toxins. The approved individual, who packages the select agent or toxin, must ensure compliance with all applicable laws concerning packaging and shipping. Guidance is available on how to package and ship select agents and toxins.

Shipment

Commercial carrier or courier: Once the package is ready for shipment, the entity should use their established procedures for providing the package to the commercial carrier. The package is not

identified as containing select agents or toxins and can be placed with other packages for pick up by commercial carrier. The transfer must comply with section 16 of the Select Agent Regulations and must be pre-authorized by the FSAP.

Hand-delivered package: While an entity may choose to hand deliver a package containing a select agent or toxin to another registered entity, it must still comply with section 16 of the Select Agent Regulations and the transfer must be pre-authorized by the FSAP. The individual who is hand carrying the package must be an individual approved by the Director, DSAT or Director, AgSAS to have access to select agents and toxins. The entity remains responsible for ensuring that all local, state or federal requirements for the transportation of hazardous materials are followed. The entity must ensure that adequate precautions are taken to prevent a theft, loss or release of the select agents and toxins.

Note: For animal or plant pathogens, interstate and certain intrastate transfers will require a valid APHIS permit.

Receipt of Packages by Entity

The entity should use their established procedures for receiving packages from the commercial carrier. It should be noted that the package containing select agents and toxins is not considered "received" by the entity until the intended recipient takes possession of the package. However, the entity should ensure that packages containing hazardous materials, including packages containing select agents and toxins, are provided to the intended recipient without delay to avoid the hazardous materials from being compromised (e.g., thawing of dry ice). For example, the entity can have the shipping and receiving personnel take the package directly to the intended recipient upon package arrival; have a secured location in the shipping area for the intended recipient to retrieve the package; or have the commercial carrier deliver the package directly to the intended recipient.

Receipt by Intended Recipient

The intended recipient or his/her designee must be an individual who is approved by the Director, DSAT or Director, AgSAS for access to select agents and toxins. Upon receipt of the shipment, the intended recipient must verify the contents. If there is a discrepancy noted, the entity must immediately notify the FSAP. The Responsible Official must complete Section 3 of the APHIS/CDC Form 2 "Request to Transfer Select Agents and Toxins" verifying receipt of the select agent or toxin and send one copy of page 2 to the sender and one copy to the FSAP within 2 business days of receipt. If the package has been damaged to the extent that a release of the select agent or toxin may have occurred, the Responsible Official must immediately report to the FSAP and complete APHIS/CDC Form 3, "Report of Theft, Loss, or Release of Select Agents and Toxins."

Security Plan

Section 11(c)(10) of the Select Agent Regulations requires that the entity's security plan contain procedures for shipping and receiving select agents and toxins. The procedures should contain documented processes to ensure select agents and toxins are safeguarded against theft, loss, intentional release or unauthorized access when a select agent or toxin is: (1) ready to be packaged for transportation, (2) packaged for shipment, or (3) received by a person with approval to access select agents and toxins. The procedures should include the following:

- How the transfer is coordinated between the sender and intended recipient;
- How the package will be tracked in transit to ensure that the intended recipient is aware of the package's expected arrival;

- How the package arrives to the intended recipient including if the individual is not available; and

- How the entity handles unexpected shipments.

If the entity temporarily stores packages identified as containing select agent or toxin at the loading dock (instead of packaged for shipment labeled generically as "Category A infectious substances" (i.e., "lost in crowd" concept)), this location must be on the entity's registration, the security plan must include how the entity temporarily stores and secures the select agents or toxins in these locations, and individuals with access to these packages must have SRA approval.

Previously all human, animal and plant infectious agents and materials, whether select agents and toxins or not, imported into the United States had to have an import permit issued by the CDC Import Permit Program, APHIS Veterinary Services, Organisms and Vectors program or the APHIS, Plant Protection and Quarantine, Plant Health Programs. In Addition, APHIS also required permits for interstate movement of all animal and plant pathogens or materials. Recently, both CDC and APHIS determined since the importation and interstate movement of select agents and toxins are regulated through the Select Agent Regulations as described above, permits would no longer be issued for BSAT's. However, both APHIS permit and CDC import permit may be required for importation of non-select agent infectious material.

Chapter 5 Quiz

CHAPTER 6: BIOSAFETY AND BIOSAFETY PLAN

OBJECTIVE: Become familiar with biosafety guidelines and how to apply them in setting up an entity biosafety program. Learn how to develop an entity specific biosafety plan that is commensurate with the risk presented by the select agents and toxins.

For self-study it is recommended that you take the Self-Evaluation Exam after you have completed reading the chapter. Compare your answers with the answers provided and review any areas were you did not provide the correct answers. If you have questions about the information provided or you have questions that are not covered by the material in this chapter contact the FSAP for assistance.

The Biosafety in Microbiological and Biomedical Laboratories (BMBL 5th ed.) and the National Institutes of Health (NIH) Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines) are the principal resources used by the FSAP to evaluate entity biosafety and biosafety programs and plans. Possessors of select toxins must also be in compliance with the Occupational Safety and Health Administration (OSHA) regulations found at 29 C.F.R. § 1910.1200 and 29 C.F.R. § 1910.1450. There are additional organizations and resources that provide information and training in biosafety and the RO should consider these resources as well when developing the entity biosafety program.

Introduction

The requirements for biosafety are specified in Section 12 of the Select Agent Regulations (42 CFR §73.12. 9 CFR §121.12, 7 CFR §331.12). Unlike the regulations for security and incident response the biosafety regulations are less specific in what is required for entity biosafety and for the entity biosafety plan. The regulation section on biosafety lists four requirements: 1) The entity that is required to register must develop and implement a written biosafety plan that is commensurate with the risk of the select agents and toxins possessed; 2) the biosafety containment facilities and equipment must be sufficient to contain the select agents and toxins; 3) the plan must include an occupational health program for individuals with access to Tier 1 agents and SARS; and 4) the plan must be reviewed annually and tested with drills and exercises.

Biosafety Plan

Biological Risk Assessment

Before writing a biosafety plan it is important to conduct a biological risk assessment. Section II – "Biological Risk Assessment", in the BMBL 5th ed. provides some information on what to consider when performing a biological risk assessment. The critical elements to consider are the hazards presented by the select agents and toxins that will be used, the work that will be performed with the agents and toxins, the facilities where the work will be done and the expertise of the individuals doing the work. The RO should involve the investigators, laboratory staff, and engineers during this process to ensure that all risks are considered. If the biosafety plan has already been written but there has never been a biological risk assessment it is recommended that one be done and compare the risk assessment with the plan to ensure that the plan covers all of the risks. It may not be possible to address every possible biosafety risk but the plan should identify and mitigate the significant risks without putting such a burden on the staff that they are not able to adhere to the plan. If the entity is planning to implement a new biological research or diagnostic program it is advisable to conduct a biological risk assessment of the program and revise the current biosafety plan or development one appropriate for the new program.

Entities are beginning to provide the biosafety plan to their staff using the entity webpage or other

electronic format. This has the advantage of being readily accessible to the staff and more convenient for making changes. If this is the format used it is important to inform the staff when changes are made and to incorporate this into the entity biosafety plan. If written plans are the format used it is advisable to have a document tracking program to ensure that when changes are made each of the plans are recalled and updated. Once a plan is developed, entities should ensure that the plan is implemented and the staff is trained on the plan. Drills and exercises should also be conducted to test the plan and modify the plan where appropriate.

The institution may have an institution biosafety plan but the biosafety plan for laboratories working with select agents and toxins must be specific to the laboratory where the select agents and toxins are used. Some institutions will have a separate biosafety plan for each principal investigator or will add an attachment to the institution plan. Whatever approach the entity takes the plan must provide the staff with instructions on the risk presented and how to mitigate the risks.

Resources

The regulations suggest three resources in developing a plan. They are:

- The CDC/NIH publication, Biosafety in Microbiological and Biomedical Laboratories."
- The Occupational Safety and Health Administration (OSHA) regulations in 29 CFR parts 1910.1200 and 1910.1450.
- The "NIH Guidelines for Research Involving Recombinant DNA Molecules."

The biosafety plan is not of much use to anyone if after it is written it is placed on the shelf and only taken down when an inspector shows up. The biosafety plan should be a living document that grows, or changes, with the entity. If a laboratory is renovated, new testing is implemented, a new research project is planned, etc., it is important to review the biosafety plan to ensure that it is still applicable. The RO must review the biosafety plan annually and must conduct drills or exercises to test the plan. Refer to Chapter 12 for information on drills and exercises. After drills or exercises the plan should be revised if indicated by the results of the drill or exercise. The entity employees should be familiar with the plan and use it frequently as a guide on how to work safely.

Plan Elements

The following is a list of elements that the RO may wish to consider in the biosafety plan. The list is not all inclusive and as stated above the entity biological risk assessment should be the guide for what is included in a plan. Every entity is different so there is no one plan that fits all entities. There should also be a biosafety plan for the care and handling of animals if animals are used at the entity. The elements for an animal biosafety plan will depend on the agents, procedures conducted, the facilities, caging and the animals used.

- Documentation of initial and annual review and approval of the plan by the appropriate individuals. This is usually the biosafety officer, principal investigator or laboratory manager, and senior management. It may also be helpful to record revisions when they are made, and briefly describe what was revised.
- A section on definitions and abbreviations used in the text of the plan.
- A statement about the importance of biosafety and the purpose of the plan.
- Roles and responsibilities of the individuals associated with biosafety.
- Training requirements.
- Description of the facilities including

information on air handling and monitoring, alarms, and communicating with engineering.

- Entry and exit procedures including personal protective equipment required.
- Waste handling procedures and autoclave operation.
- Biosafety cabinet use.
- Medical surveillance program and requirements for fit testing, respiratory evaluation, immunizations, etc. This can be part of the entity occupational health plan and a separate document of an appendix to the biosafety plan.
- Accident and spill procedures.
- Escorting visitors, maintenance and cleaning staff.
- Descriptions of agents used including hazards and symptoms of exposure.
- Preparation and use of disinfectants including full room disinfection.
- Packaging agents for shipment and receiving agents or diagnostic specimens.
- Operation of aerosol generating equipment, centrifuges, shakers, vacuum systems, etc.
- Use and disposal of sharps.
- Notification of biosafety hazards.
- Approvals for use of agents and toxins.

Some entities will use standard operation procedures (SOPs) and in this case the biosafety plan should make reference to the SOPs and where they can be accessed. If the plan is part of a larger institution wide plan this should be referenced.

Biosafety

The biosafety practices and the physical containment must be sufficient to prevent the select agents and toxins from putting the laboratory staff and the public at risk. As stated before a risk assessment is critical in determining the biosafety practices and the physical containment required. There are guidelines on the type of containment (BSL-2, 3, 4) appropriate for specific agents and while these are useful for general program development the RO should not select a level of containment just based on the agent to be used. It is important to also consider the other risk factors listed above namely, how the agents are used, competency of laboratory staff, equipment requirements, personal protective equipment used, use of animals, and facility support available. The RO should also consider the information that is provided in Chapter 14 - "Facilities: Commissioning and Verification".

In developing and maintaining a biosafety program the RO should involve the laboratory staff, engineers, veterinarians, and biosafety personnel. Research institutions should have an active institutional biosafety committee that meets regularly to review the biosafety requirements for new research projects, establish entity biosafety practices and policies and respond to biosafety issues. If the RO does not have expertise in biosafety the entity should consider recruiting a person trained in biosafety or develop the expertise in an existing employee. In some institutions this person may be part of the environmental health office. This position can be part time, or full time depending on the size of the entity, and should include biological safety for all infectious disease agents not just select agents. There is no requirement that the RO be an expert in biosafety but if the RO does not have expertise in biosafety the RO and the biosafety official should have a close working relationship.

Occupational Health Program

A requirement that was added to the October 2012 amendments to the Select Agent Regulations is the inclusion of an occupational health program for individuals with access to Tier 1 select agents and toxins and to SARS. The FSAP has published a guidance document, "Occupational Health Program Guidance Document for Working with Tier 1 Select Agents and Toxins." While the requirement is for those entities with Tier 1 agents, it is recommended that any entity with infectious disease agents and hazardous chemicals have an occupational health program. The FSAP has expertise in occupational health programs and the RO can contact their assigned file manager who can assist in making this expertise available.

Chapter 6 Quiz

CHAPTER 7: SECURITY AND THE SECURITY PLAN

OBJECTIVE: Learn the requirements for entity security, how to assess security risk, how to develop a security plan, and procedures for obtaining an SRA.

For self-study it is recommended that you take the Self-Evaluation Exam after you have completed reading the chapter. Compare your answers with the answers provided and review any areas were you did not provide the correct answers. If you have questions about the information provided or you have questions that are not covered by the material in this chapter contact the FSAP for assistance.

For information on the security risk assessment (SRA) process and instructions on completing the FD-961 go to the FBI website at http:/www.fbi.gov/terrorinfo/bioterrorfd961.htm. You can also contact CJIS directly at 304-625-4900. The FSAP has security experts available to discuss security requirements and issues. Guidance for Suitability Assessments, Information Systems Security Control Guidance Document, Security Guidance for Select Agent or Toxin Facilities, and Security Risk Assessments Tool contain guidance related to security requirements.

Introduction

A major change to the amended regulations, published October 5, 2012, was in the area of security. The amended regulations contain security requirements that took effect on April 3, 2013. The requirements include enhancements to the security plan, specifications for when the entity must conduct a complete inventory audit, establishment of a higher level security for specified select agents and toxins ("Tier 1"), requirement for a personal reliability program for entities with Tier 1 BSAT, requirement for additional security barriers for Tier 1 BSAT, and additional security responsibilities assigned to the RO. The two sections in the Select Agent Regulations that prescribe security requirements are Section 10 – Restricting access to select agents and toxins; security risk assessments and Section 11 – Security (42 CFR §73.10 and §73.11, 7 CFR §331.10 and §331.11, 9 CFR §121.10 and § 121.11). Changes to Section 10 took effect on December 4, 2012 and changes to Section 11 took effect on April 3, 2013.

This chapter covers the Security Risk Assessment (SRA), physical security, the security plan, and Tier 1 security requirements.

Security Risk Assessment

General Information

One of the fundamental elements of security for select agents and toxin is preventing access to these materials by individuals who intentionally or unintentionally would use them to place humans, animal, or domestic plants at risk. The Select Agent Regulations state that an individual will be deemed to have access to select agents and toxins at any point in time if the individual has possession of a select agent or toxin (ability to carry, use or manipulate) or the ability to gain possession of a select agent or toxin. The FSAP works closely with the Federal Bureau of Investigation's Criminal Justice Information Services (CJIS) to identity those individuals who are prohibited from access to select agents and toxins based on restrictions listed in Section 175b(d)(2) of title 18 of the U.S. Code. CJIS conducts security risk assessments of all individuals, including, but not limited to, Responsible Officials, Alternate Responsible Officials, corporate officials, and non-government entities who request approval for access to select agents and toxins. CJIS conducts a review or security risk assessment of the individual or entity against a series of criminal and law enforcement data bases to determine if the individual or entity meets any of the restrictions listed in section 175b.

CJIS notifies either the DSAT or AgSAS as to whether the person meets one of the restriction criteria and the DSAT or AgSAS select agent program determines, and notifies the entity and the individual, if the individual or entity should be allowed to have access to select agents and toxins. The SRA is valid for a period of up to three years. The SRA is not transferable. Individuals who move from one entity to another must reapply for an SRA but they are not required to resubmit fingerprints unless requested by CJIS.

Restricted Person

A restricted person is defined as anyone who:

- Is under indictment for a crime punishable by imprisonment for a term exceeding one year;
- Has been convicted in any court of a crime punishable by imprisonment for a term exceeding 1 year; (Note the person may not actually spend a year in prison but if the crime committed would have resulted in imprisonment for over a year they are still considered a restricted person)
- Is a fugitive from justice;
- Is an unlawful user of any controlled substance (as defined in section 102 of the Controlled Substances Act (21 U.S.C 802));
- Is an alien illegally or unlawfully in the United States;
- Has been adjudicated as a mental defective or has been committed to any mental institution;
- Is an alien (other than an alien lawfully admitted for permanent residence) who is a national of a country to which the Secretary of State has made a determination (that remains in effect) that such country has repeatedly provided support for acts of international terrorism; or acts for or on behalf of, or operates subject to the direction or control of, a government or official of such a country (Note: the countries so designated are: Cuba, Iran, the Republic of Sudan and Syria);
- Has been discharged from the Armed Services of the United States under dishonorable conditions;
- Is a member of, acts for or on behalf of, or operates subject to the direction or control of, a terrorist organization as defined in section 212(a)(3)(B)(vi) of the Immigration and Nationality Act.

Furthermore, the Director, DSAT and the Director, AgSAS, may limit or deny access to such agents and toxins by individuals whom the CJIS has identified as within one of the following categories;

- The individual is reasonably suspected by a Federal law enforcement, or intelligence agency, of committing a crime as set forth in 18 USC 2332b(g)(5);
- The individual is knowingly involvement with an organization that engages in domestic or international terrorism (as defined in 28 USC 2331, or with any other organization that engages in intentional crimes of violence; or
- The individual is an agent of a foreign power as defined in 50 USC 1801.

"Federal Select Agent Program Guidance on an Individual who has been identified as a Restricted Person" provides guidance on restricted persons.

Physical Security

Physical security refers to the measures put in place to prevent unauthorized individuals from gaining access to the BSAT. Development of physical security requires a through security risk assessment to be conducted before implementing the necessary security measures. This is important to ensure that the security necessary to protect the BSAT is implemented and it serves to prevent the implementation of unnecessary, and expensive,

security measures. It can also ensure that the security requirements are reasonable within light of the risks and the mission of the entity. Security measures that do not make sense to the personnel, or that impede critical entity programs, are less likely to be supported by the personnel, or by the institution management. If a physical security system is already in place conducting a risk assessment can prove valuable in identifying gaps in the system and it can also be helpful in gaining an understanding of all aspects of the entity's security.

The regulations do not require the RO to be an expert in security but the RO must be familiar with the security requirements. There are security resources available to the RO, many of which may be in the RO's institution or community. The FSAP provides a guidance document, "Security Guidance for Select Agent or Toxin Facilities." This guidance document provides information on the elements to consider when developing an effective security system. Also included on the FSAP web site is a security risk assessment tool that can be used to assist an entity in performing this assessment. The FSAP has security specialists available who can assist RO's with questions about security requirements. The RO who wishes to access this service should contact their FSAP assigned file manager. There are also other resources that the RO may have access to. These include the institution security office (e.g. campus police) local public safety (city, county or state), the Federal Bureau of Investigation Weapons of Mass Destruction regional office in the entity's area and commercial security firms that do risk assessments.

Security Plan

Every registered entity must have a security plan and the plan must be based on a site specific security risk assessment. A plan that is developed without the benefit of a security risk assessment runs the risk of not being sufficient to safeguard the select agents or toxins against unauthorized access, theft, loss or release and will fail to provide the graded protection required. If the plan has already been developed the security risk assessment should be used to evaluate the security plan for gaps in security coverage. While the security plan must be based on the entity specific risk assessment the regulations specify certain elements that must be in the plan. These are the following:

- Describe the entity physical security. This should include a description of the security barriers in place such as fences, access point controls, alarms, vehicle barriers, video monitoring systems, and guard monitoring. This may be part of the overall institutional security policies and procedures, and reference should be made to these documents if that is the case. The entity may consider some of the information sensitive and have limited distribution for the detailed description with a more general description in the more widely distributed plan. The plan that is made available to the staff should be sufficient to ensure the staff is engaged in protecting the BSAT from theft, or loss.

- Describe procedures for control of the long term inventory of select agents and toxins. "Guidance for the Inventory Requirements for Select Agents and Toxins" provides more details on how to create a secure inventory system.

- Describe procedures for information systems control. Assistance in understanding the requirements and developing measures to meet the requirements can be found in the guidance document "Information Systems Security Control Guidance Document."

- Describe the control of access to and safeguarding of animals, plants or arthropods that have been exposed, or may have potentially been exposed. There should be a description of the procedures for dealing with escaped animals especially ones that are able to get out of containment and possibly into the community. This is also an important component of the entity incident response plan.

- Describe procedures for ensuring security when the laboratory must be cleaned, or maintenance and repairs must be done. The description should provide information on how access is granted to the cleaning and maintenance and repair personnel, how access is recorded, how the select agents and toxins will be secured when these individuals are present and provisions for escort during the procedures if required.

- Contain procedures for identifying and removing unauthorized individuals.

- Describe the procedures for responding to a loss of keys, access cards or compromise of access codes. This should include who personnel should notify in the event of loss, what procedures should be taken to change locks or reprogram access systems. It also includes procedures for how individuals obtain access; who authorizes access and who programs the card or provides keys. Procedures for removing access and collecting cards or keys from individuals who leave the entity should also be described.

- Describe procedures for responding to the theft, or loss of select agents and toxins or for the discovery of inventory record alterations. "Guidance for the Inventory Requirements for Select Agents and Toxins" provides additional information.

- Contain provisions for ensuring that everyone with access to select agents and toxins have been informed and trained on the security requirements. Security drills and exercises are an excellent way to make entity personnel aware of security policies and procedures.

It is important to review the security plan with security personnel at least once a year. If there are changes to the entity, such as the addition of new projects, renovation of facilities, or if the security office makes changes to their policies and procedures the physical security and the security plan should be reviewed. If the facility is undergoing renovation it may be advisable to have security procedures for the coming and going of construction personnel and consideration should be given to providing instructions on the entity general security precautions. The reason for taking this under consideration is that the normal security barriers may change during construction, and alarm systems and visual monitoring systems may have been disabled.

Tier 1 Security

The amendments to the regulations published in October 2012 identify a subset of the list of select agents and toxins which are deemed to have a greater public health or animal health risk and therefore require additional security. These are referred to in the regulations as "Tier 1" agents. The entity must:

- Establish procedures for conducting personal suitability assessments for individuals who will have access to Tier 1 agents and toxins. Individuals, who have had access to Tier 1 agents and toxins before April 3, 2013 when the Tier 1 part of the regulations took effect, do not have to have an initial personal suitability assessment. The personal suitability assessment is an evaluation of the individual to determine if they should have access to Tier 1 agents and toxins. This is not in place of the SRA.

- Establish procedures for how the RO will share information on security issues and coordinate security efforts with the entity's safety and security professionals. In the case of entities that do not have security and/or safety professionals the RO may wish to establish contact with the local public safety (police) or the FBI's Weapons of Mass Destruction regional office to discuss ways to implement this.

- Establish procedures for ongoing assessment of the suitability of personnel to have access to Tier 1 agents and toxins. This involves training of entity staff on reporting, evaluating and

correcting actions of an individual that raise concerns about an individual having access to Tier 1 agents and toxins.

- Implement enhancements to current security physical security and security procedures.

"Guidance for Suitability Assessments" and "Security Guidance for Select Agent or Toxins Facilities" contain information on how the RO can address the Tier 1 requirements. There are also security specialists in the FSAP who can provide advice in this area. The RO should contact their File Manager if they wish to speak with one of the security specialists.

Chapter 7 Quiz

CHAPTER 8: INCIDENT RESPONSE PLAN

OBJECTIVE: To gain an understanding of how to develop an incident response plan that meets the regulatory requirements and that prepares the entity for potential natural, or man-made, disasters.

For self-study it is recommended that you take the Self-Evaluation Exam after you have completed reading the chapter. Compare your answers with the answers provided and review any areas where you did not provide the correct answers. If you have questions about the information provided or you have questions that are not covered by the material in this chapter contact the FSAP for assistance.

The "Incident Response Plan Guidance Document" provides information helpful in developing an entity incident response plan. The FSAP also has personnel with expertise in emergency planning and the RO should contact their file manager to access this resource.

Introduction

The Select Agent Regulations specify in 7 CFR §331.14, 9 CFR §121.14 and 42 CFR §73.14 that a requirement for registration with the Federal Select Agent Program (FSAP) is the entity must develop and implement a written incident response plan. The purpose of this chapter is to provide an overview of the regulatory requirements in regards to incident response and to note the amendments to Select Agent Regulations that became effective April 3, 2013 having to do with incident response. The Incident Response Plan Guidance Document that is mentioned above is an excellent resource for how to implement the regulatory requirements. This chapter is not intended to duplicate the information that is in the guidance document but to point out the requirements for an incident response plan. The guidance document in the appendix provides information that a RO should consider when developing the entity plan or reviewing a current plan.

The entity incident response plan is expected to provide the measures that would be implemented to mitigate the natural and man-made threats to which the entity may be subjected. No plan will anticipate and adequately plan for every possible emergency; however, a well designed and implemented plan should reduce the impact of the emergency and result in more rapid recovery after an incident.

The incident response plan previously referred to as an "emergency response plan" may also be called the "business continuity plan" by some entities. There may be community wide emergency response plans, company or campus plans and department plans and these should be considered before developing the select agent incident response plan which is very specific to select agent and toxins. This will avoid confusion, duplication and possible conflicting plans. Some entities may choose to establish a collection of standard operating procedures instead of a single document. If this is the approach it is important that the entity identify and organize the standard operating procedures as the entity incident response procedures and ensure that all the regulatory requirements are addressed.

Requirements

The entity response plan must be based on a site specific risk assessment. This is a new requirement. The entity is required to determine the natural and man-made threats to which the entity might be subjected to, and what measures are in place to mitigate the threats. The entity should coordinate the select agent specific plan with entity-wide plans. In the case of a military installation, a university campus, or corporation the select agent specific plan should be in coordination with the institution incident response plan. In the case of a smaller entity where there may not be an institution wide plan the entity should explore the resources available in the local

community and determine how it could benefit from coordination with the community resources. There is additional information in the guidance document on resources for potential disasters in the entity's region. The incident response plan should be kept in the workplace and available for review by employees. Training on the plan and incident response drills and exercises are important components of the overall entity's incident response planning.

The entity is required to fully describe the response to a theft, loss or release of a select agent or toxin, the response to an inventory discrepancy, breaches in security such as a break-in, access to select agents by an unauthorized person, and unauthorized access to information technology systems. The plan must describe responses to the types of severe weather and natural disasters the entity may be subjected to given the entity location. The plan must describe how it will respond to workplace violence, bomb threats, or how suspicious packages will be identified and handled. The plan must also include responses to fire, gas leak, explosion, and power outages. Entities that maintain animal colonies must include how the animals infected with select agents will be handled under emergency circumstances. Since there will be different responses depending on the type of incident it is important that the plan fully describe the response for each type of incident. It is not necessary to include incidents in the plan that have a very low probability of occurring or would have low impact but if they would have a high impact (severe consequence), even if a low probability, they should be included in the plan. An example is an entity in an area where hurricanes are not known to occur (low probability) but the entity works with foot-and-mouth disease virus and the release of infected animals would have high consequences.

The regulations also contain the requirement that the entity describe how it will respond if the select agents and toxins, or infected animals, including arthropods, are released during a disaster. The release may be to the laboratory, the building or the community. The RO should consider and incorporate into the plan, if appropriate, what procedures would be implemented under varying scenarios and who should be involved. The plan must also take into account the impact of the release of plant pathogens if the entity possesses plant pathogens, and the impact on animals and animal products if the entity works with animals.

Other information that must be in the plan is:

Contact Information

- The name and contact information (home, cell phone, work, etc.) for the Responsible Official, Alternate Responsible Official(s) and biosafety officer. If there are other individuals who are involved in the response such as animal care staff, laboratorians, and engineers, they should also be listed. Depending on the type of emergency the individuals to be contacted may vary and if this is the case the plan should note this. It is also important to ensure that names and contact information are updated anytime there is a change. An emergency is not the time to find out that the contact list is out of date.

- The name and contact information for the building owner and/or manager, where applicable, must be included. Depending on the entity this could be the facilities engineer, the physical plant office, or some other contact. It is important for the RO to identify who is responsible for the laboratory buildings so in an emergency he/she knows who to contact to do such things as shut off, or restart utilities, and provide building information to emergency responders.

- The name and contact information for tenant offices, where applicable. For military entities this may be the base command, for a university campus probably the building and grounds or facilities management office, for public health departments it may be the state building and grounds department. The RO should record the name of the person who is responsible for

the building where the laboratories are located, record contact information and describe the role of the building tenant responsible person in emergencies.

- The name and contact information for the physical security official for the building. This is important information because security will have to be involved in keeping the select agents and toxins and facilities secure in an emergency situation and responding to security incidents such as a theft or bomb threat. If the security is provided by a contractor there should be a point of contact listed. If local public safety organizations (police, fire, HAZMAT) are part of the incident response plan contact information should be included. It is also suggest that the contact for the regional Federal Bureau of Investigation, Weapons of Mass Destruction office be listed.

Other Information

- Personnel roles and lines of authority and communication. It is important for the incident response plan to describe the roles of each of the individuals responsible for responding to an emergency and the role they play in the response. There will probably be different personnel and roles depending on the incident. For example, the individuals who respond to a spill in the laboratory may be different and have a different role than the individuals who respond to an incident in the animal care facility. The RO may also wish to consider having a back-up system for communication during an incident. The normal communication systems may be disrupted during a natural hazard such as a hurricane for example, and alternatives should be available.

- Planning and coordination with local emergency responders. Local emergency responders may be the campus fire department, the community fire department, the state emergency preparedness department or all of these. Using the incident risk assessment the RO can determine who the coordination should be with and the role they play. Some entities make a habit of including local responders in the entity drills and exercises and this is especially important if they are first responders to an incident.

- Procedures to be followed by employees performing rescue or medical duties. The entity incident plan is expected to contain information, or refer to the source of information, on the procedures to be followed for rescuing and providing medical care in the case of an incident. This requirement may be met in different ways by entities. Some entities may have their own trained response team while others may require all members of the staff to be trained to perform rescue and medical duties. Regardless of how the entity approaches this, a description of who is responsible and how rescue and medical duties are carried out must be either in the plan or there must be reference to a document, such as a standard operation procedure, that provides the information.

- A list of personal protective and emergency equipment, and their locations. The plan is expected to identify the equipment necessary to respond to emergencies and where it is located. This would include such things as spill kits, personal protective equipment necessary to enter the laboratory, fire blankets, personnel removal devices, disinfectant, etc. It is suggested that the entity identify these locations by signage or other means so responders can quickly identify where to find the equipment. The RO should periodically check the equipment and supplies to ensure that the necessary equipment is available and usable. Don't neglect to consider access to the equipment in the event the lights go out.

- Site security and control. The plan should identify the security that will be implemented in an emergency. This will probably vary depending on the type of emergency. This information may be in the security plan. If that is the case then the incident response plan should reference the specific part of the security plan that addresses this requirement.

- Procedures for emergency evacuation, including type of evacuation, exit route assignments, safe distances, and places of refuge. The plan should describe the responses to each kind of emergency. In some cases evacuation may not be the appropriate action or the place of refuge will be different for different emergencies. In some cases it may be necessary to not only consider evacuation of the building or campus but also the area and coordination with community evaluation plans may be appropriate. If evacuation is the required response there should be procedures for ensuring that all the personnel are accounted for.

- Emergency medical treatment and first aid. The plan is expected to contain a description of emergency medical treatment and first aid if any would be given.

- Decontamination procedures. The plan is expected to contain a description of the decontamination of the areas that have been impacted. This would include the circumstances where decontamination is required, what kind of decontamination would be used, who is responsible for the decontamination, and how is the area verified to be safe for re-entry.

Requirements for Tier 1

For those entities that possess Tier 1 agents and toxins there are two additional requirements. The incident response plan must describe the entity's response in the case of failure of intrusion detection systems such as locks, cameras, alarms or other means of deterring or recording unauthorized entry. This may be described in the entity security plan but if this is the case the incident response plan should reference the part of the security plan that addresses this.

The other requirement is a description for how the entity will notify the appropriate Federal, State, or local law enforcement agencies of suspicious activity that may be criminal in nature and related to the entity, its personnel, or its select agents or toxins. This may be such things as employees bringing firearms to work, unusual interest in entity activities by outsiders, individuals removing select agents and toxins from authorized areas, or employees stealing supplies and equipment. The regional FBI Weapons of Mass Destruction office may be helpful to the RO in how this requirement can be met.

The incident response plan must be reviewed at least annually and revised if necessary. It is important for the RO to document this annual review and note any changes. It is also important to test the plan by conducting drills or exercises. Drills and exercises are also an excellent way to train staff on the plan and to detect gaps in the plan.

Chapter 8 Quiz

CHAPTER 9: RESTRICTED EXPERIMENTS, EXEMPTIONS, AND EXCLUSIONS

OBJECTIVE: To become familiar with the term "Restricted Experiment", as used in the Select Agent Regulations, the types of restricted experiments, and how to request approval to conduct experiments that require approval. Be able to distinguish between exemptions and exclusions and the requirements for each category.

For self-study it is recommended that you take the Self-Evaluation Exam after you have completed reading the chapter. Compare your answers with the answers provided and review any areas were your answers were not in agreement. If you have questions about the information provided or you have questions that are not covered by the material in this chapter contact the FSAP for assistance.

Restricted Experiments Guidance contains information intended to assist the RO in meeting the restricted experiment regulatory requirements. Select Agent and Toxin Exclusions contain guidance on applying for exclusions. Synthetic Genomics Guidance contains information on synthetic genomics.

Introduction

This chapter provides information about the regulatory requirements regarding restricted experiments defined in Section 13 of the Select Agent Regulations (42 CFR §73.13, 9 CFR §121.13, 7 CFR §331.13). Also included in this chapter is information on exemptions defined in sections 5 and 6 (42 CFR §73.5 and §73.6, 9 CFR §121.5 and §121.6 and CFR §331.5) and exclusions defined in Section 3 and 4 (42 CFR §73.3 and §73.4, 9 CFR §121.3 and §121.4 and 7 CFR §331.3). Restricted experiments and exemptions and exclusions are very different subjects but for convenience they have been included together in this chapter. It is important for the RO to be familiar with how to identify research that involves restricted experiments and what is required to obtain approval for these kinds of experiments. The RO should also be familiar with the difference between exemptions and exclusions and the requirements for each.

Restricted Experiments

The term, "Restricted Experiments" is used in the regulations to identify experiments that require review and approval before the entity is allowed to conduct the experiments. There are two types of restricted experiments. One type is an experiment that involves select agents where there is a deliberate transfer or selection for, a drug resistance trait in the select agent that is not known to acquire the trait naturally if the acquisition of the trait could compromise the control of the select agent in humans, animals or plants. An example would be an experiment that resulted in selection of a strain of *Francisella tularensis* resistant to tetracyclines, which are first line drugs for treatment of tularemia or development of a strain of *Brucella abortus* that would not be susceptible to the drugs used to treat animals.

The other type of experiment involves the deliberate formation of synthetic or recombinant nucleic acids containing genes for the biosynthesis of a select toxins lethal for vertebrates at an LD[50] of less than 100ng/kg body weight.

The RO should make it a point to be familiar with all of the research that is conducted at their entity using select agents and toxins and be involved in the institution's biosafety committee if there is one. If the RO has recently joined the institution one of the first tasks should be to talk with each researcher about their research program. The RO should also provide information to assist researchers in

understanding the Select Agent Regulations and the requirements for restricted experiment approval.

Entities that wish to conduct research involving experiments identified as restricted are expected to request approval from the FSAP prior to initiating any of the proposed work. For information on how to submit a request for a restricted experiment and what information is needed please consult the restricted experiment guidance document. If the RO is not sure that an experiment is restricted, the RO should contact the FSAP to discuss and receive guidance. The guidance documents mentioned above provide instructions on how to submit a request for approval to conduct a restricted experiment. It is important that the information be comprehensive and detailed with extensive reference to related work.

Exemptions

The select agent regulatory exemptions provide that individuals or entities that may find themselves in possession of a select agent or toxins are not required to be in compliance with the select agent regulations for so long as they take the specific actions required and/or meet the specific conditions proscribed by the regulations in section 5 or section 6. The current exemptions provided for in the regulations are for (1) diagnostic, verification, or proficiency testing specimens in clinical or diagnostic laboratories, (2) products licensed or otherwise approved for use by the Federal government under specific statutes, (3) investigational products approved by the Federal government under specific statutes, and (4) when either the HHS Secretary or the APHIS Administrator may grant specific exemptions due to a public health or agricultural emergency, respectively.

Exclusions

The select agent regulatory exclusions list the circumstances under which the select agent regulations do not apply to the possession, use, or transfer of select agents or listed in the select agent regulations. Excluded attenuated strains or toxins are not subject to the requirements of the select agent regulations. An entity may request that a biological agent or toxin be excluded by submitting a letter with supporting documentation to the FSAP. Guidance is available on how to apply for an exclusion. If the RO is not sure whether a BSAT has been excluded, he/she should contact the FSAP.

Chapter 9 Quiz

CHAPTER 10: RECORDS

OBJECTIVE: To become familiar with the records that an entity must maintain as specified in the Select Agent Regulations.

For self-study it is recommended that you take the Self-Evaluation Exam after you have completed reading the chapter. Compare your answers with the answers provided and review any areas where you did not provide the correct answers. If you have questions about the information provided or you have questions that are not covered by the material in this chapter contact the FSAP for assistance.

The record requirements in the Select Agent Regulations (42 CFR §73, 9 CFR §121 and 7 CFR §331) are found primarily in Section 17, although other sections of the regulations contain record keeping requirements.

Introduction

The creation and maintenance of records that document the select agent activities at the entity are an essential part of the RO's responsibilities. If the RO does not maintain records of select agent activities it is difficult to verify that the entity is in compliance with the Select Agent Regulations. The records must be accurate, comprehensive, current and organized so they can be readily produced if requested by FSAP inspectors. The records must also be maintained securely to prevent unauthorized removal or alteration of the records. The records that must be maintained are described throughout the Select Agent Regulations. This chapter lists all of the records that are either required or highly recommended to be maintained and a description of the contents of the records. All records must be maintained for a period of at least three years but entity policy may dictate longer retention times. Records and documents can be maintained electronically or hard copy or by both methods. It is advisable for the RO to keep backup copies of any records pertaining to the entity select agent and toxin activities and to store the records in a manner that reduces the risk of loss. It is advisable for the RO to make copies of any documents submitted to the FSAP.

Description of Required Records

Application and Amendments

The RO should maintain a file of the application for registration and any amendments to the application. The RO will be requested to submit a complete application prior to renewal. The previous application should be retained for three years so in effect the RO has a copy of the most recent application and a copy of the previous application at all times. Any correspondence associated with an application or an amendment should also be maintained in the event there is a question about what occurred. These records are also valuable if there is a change in the RO to ensure continuity of the entity select agent compliance program. One of the first things that a new RO should do is to review the current application documents. This is a very quick way for the new RO to become familiar with the entity's select agent program.

List of Select Agents and Toxins

The select agents and toxins the entity is registered for are listed in the entity application and will also be listed in amendments adding agents and toxins but it is important for the RO to maintain a record of what select agents and toxins the entity is registered for and to ensure that the entity inventory is consistent with the agents the entity is authorized to possess. The RO should have a means of maintaining a current inventory, either electronic or paper, that details what select agents and toxins are at the entity and where they are located. This inventory should be updated frequently and periodic audits should be conducted as either spot checks or full inventory audits. For the entity with an extensive collection of select agents and toxins this can be a daunting task but there are systems

that provide efficiency and ease in maintaining large inventories. There are electronic systems commercially available but some entities choose to develop their own systems.

An entity may discover select agents or toxins in unregistered space. This may be the result of work that was done in the past and the researcher has left the institution, or a researcher is not aware of what agents are select agents. If a discovery is made of agents for which the entity is not registered, or that are stored in unregistered space, the RO should immediately secure the BSAT and notify the FSAP. The RO should be aware of all biological research and diagnostic activities at their entity. This may involve visiting all of the institution's laboratories and storage areas, attending research presentations, communicating select agent regulations at institution meetings, asking questions and looking at research records, reports and scientific articles published by the entity.

Some entities choose to consolidate all inventories into one location while others choose to allow researchers to control their own inventories. For entities that have small inventories and only a few researchers this is not a particularly difficult issue. For large inventories and multiple inventories this can be more challenging. The advantage of a centralized inventory is it allows better control of the select agent and toxins possessed by the entity and it is easier to maintain security. The disadvantage is it is inconvenient for the researcher and it does not give the researcher a sense that they control their own collection. However the entity chooses to handle their select agent and toxin inventories it is important to adopt inventory policies and procedures that reduce the risk of a theft or loss of select agents and toxins possessed by the entity.

Internal Audits

The RO is expected to conduct annual internal audits to ensure that the entity is meeting all of the regulatory requirements. The RO can develop their own system or can incorporate the FSAP inspection checklists which are used by FSAP inspectors when they conduct an onsite inspection. Unfortunately the checklists are not in a form that can be altered by the RO but they can be used by the RO to develop their own entity specific checklists. The RO should maintain a copy of the internal audits, documentation of the deficiencies noted and documentation of the resolution of the deficiencies. The RO may need to produce these records during an FSAP inspection.

The internal audits should include an audit of the inventory. The question has been raised regarding how often an inventory audit should be conducted. This depends on the entity but if the inventory is rarely accessed then an annual audit is probably sufficient but if there is frequent access to the inventory the audits should be more frequent. Records should be maintained of the inventory audits which describe who conducted the audit, how many units were examined, when the audit was conducted, whether there were any discrepancies and what was done about the discrepancies. Any inventory discrepancy must be immediately reported to the FSAP. Refer to Chapter 4 - Reporting, for more information on reporting an inventory discrepancy. It is recommended that the RO perform the inventory audit, or be present during the audit, rather than ask the PI or laboratory manager to conduct the audit as this helps to ensure that any discrepancies are addressed and required notifications are made.

Security Risk Assessment

The RO should maintain a record of all individuals that have a Security Risk Assessment (SRA). The record should contain the name of the individual, when they submitted a request for a SRA, when they were approved, when they were allowed access to select agents toxins, and when the SRA expires. The SRA expires three years after approval. The FSAP will notify the RO prior to the expiration of a person's SRA but it is the ultimate responsibility of the RO to ensure that a person whose SRA has expired is not allowed access to select agents and toxins. The renewal request for a SRA should be submitted at least 45 days before expiration.

Record of Access

The RO is expected to ensure there is a record of who has access to rooms where select agents are used and stored. There should be a frequent review to ensure that only individuals with a SRA, or who are escorted by a person with a SRA, have access to the rooms where select agents and toxins are used and stored. Some entities have electronic print outs, some have manual logs and some entities have both. However the entity chooses to record access the records, like all select agent related records, must be maintained for three years. It is common for inspectors to check the access records against the list of SRA approved individuals when conducting an inspection.

Training

There should be a training record established for each person who is granted access to the select agent and toxins. The record should include the person's name, position, when they were hired, the date of each training they received, a description of the training and the means used to verify that the individual understood the training. It is recommended that the RO also note when the individual received an approved SRA and when they were given access to select agents and toxins. Refresher training is required annually and this must also be documented. The RO is also expected to maintain records of the training provided to individuals without an SRA that are escorted into areas where the select agents and toxins are used and stored. See Chapter 11 for additional information on the requirements for training. Entities with Tier 1 agents are required to provide security awareness training annually to those individuals who have access to Tier 1 agents. This training should be documented.

Biosafety, Security and Incident Response Plans

The entity is required to maintain current biosafety, security and incident response plans that are reviewed at least annually. A record of the annual review and any modifications to the plans should be maintained. The FSAP may request updated plans during inspections, upon changes to the entities' registration or at the time of the entities registration renewal.

Entry Requirements

If the entity requires immunizations, base line sera, respiratory evaluations and fit testing, or health evaluations records these should be maintained. Since these records contain sensitive personal information the entity policy may dictate that these records are kept by the entity occupational health service. The RO is not required to maintain these records if that is against institution policy but the RO is expected to ensure that those responsible for the records understand that the records must be complete and accurate and provide a means of verifying that individuals requiring immunizations, tests, etc. have met all of the entity requirements for work in the laboratories.

FSAP Inspection Reports

It is advisable that the RO maintain previous FSAP inspection reports including the response to deficiencies and all related follow-up documentation. The benefit of maintaining these reports is the RO can review the report prior to a FSAP inspection to confirm that all previous inspection deficiencies were resolved and the records provide information continuity when there is a change in the entity RO. The RO should ensure that previous inspection deficiencies have been corrected as the entity has stated.

Commissioning and Verification Documents

The original commissioning documentation of high and maximum containment laboratories should be maintained. Subsequent annual verification documentation of the containment laboratories should also be maintained. The RO should expect to produce the documents during an inspection. These records may be maintained by the facilities manager or engineer but it is the responsibility of the RO to ensure these records are maintained and

are complete. Refer to Chapter 14 for additional information on facilities.

Equipment Records

Biological Safety Cabinet (BSC), Autoclaves, Digesters, Liquid Decontamination Systems (LDS), Heating, Ventilation and Air Conditioning (HVAC), High-efficiency particulate air (HEPA): Maintenance records for the biological safety cabinets that include the cabinet identification, the maintenance conducted, and date of certification should be maintained. Maintenance records for the autoclaves, digesters, HEPA filters, exhaust fans and other laboratory equipment should be maintained. Records of sterilization verification for autoclaves and decontamination verification for digesters and liquid effluent decontamination systems should be maintained along with maintenance records.

Certifications and External Inspections/Audits

Inspections, reviews, certifications or audits by other agencies, or groups should be maintained. There are no specific regulatory requirements to maintain these documents however if they are maintained for an extended time period they provide continuity perspective and they may be useful in responding to FSAP inquires and inspection deficiencies.

IBC Minutes

If there is an Institutional Biosafety Committee (IBC) inspectors may ask to look at the committee minutes. There is no requirement under the Select Agent Regulations that there be an IBC.

Transfers

All records of transfers of select agents and toxins into the entity and from the entity must be maintained. These are the APHIS/CDC Form 2 documents that are described in Chapter 5. It is advisable to include with the APHIS/CDC Form 2 all shipping invoices and related materials. Records of transfers of select agents and toxins within the entity should also be maintained. These are records of the transfer of select agents and toxins between investigators in the same entity. Some entities have developed their own internal transfer form for tracking these events. The RO should ensure that the internal transfer records and the APHIS/CDC Form 2 records are consistent with the inventory records.

Reports of Identification of Select Agents and Toxins

Reporting the identification of select agents and toxins using APHIS/CDC Form 4 was described in Chapter 4 – Reporting Requirements. Copies of the reports to the FSAP should be maintained.

Reports of Theft, Loss and Release

Reporting of a theft loss or release of a select agent or toxin using APHIS/CDC Form 3 was described in Chapter 4 – Reporting Requirements. Copies of these reports and any related follow-up documents should be maintained for at least three years.

Security

As part of the security provisions the RO should ensure that there is a record of who have been assigned codes, keys, combinations, and other access equipment. If this is kept by the entity security officer the RO should establish a system of periodically checking these records to ensure that only SRA approved individuals have been given access to restricted areas. These records should also reflect the dates when access was removed in order to establish a real time record of individuals who are accessing select agents and toxins at the entity.

Requests for Restricted Experiments

All documentation related to the entity's submission of a request to conduct restricted experiments should be maintained. This includes the letter requesting the review, all supportive documents and all related correspondence. While the records must be maintained for a minimum of three years it is advisable that the records be kept as long as the research is being conducted if it continues past three years.

Drills/exercises

Drills and exercises to test the security, safety and incident response plans are required to be conducted annually. These are described in Chapter 12. It is not required but maintaining records of the drills or exercises including, a list of the participants, the date the drill or exercise was conducted, the outcome and any corrections made as a result can be helpful for future planning.

Additional Records

The records described in this chapter are those that the RO is required to maintain or that should maintain. Required records must be maintained for at least three years and should be kept secure to avoid any loss or alternation. Any documents related to activities at the entity which are related to the possession, use and transfer of select agents and toxins not listed above should also be maintained by the RO. Maintaining an organized record system that involves frequent review and updating can avoid problems during FSAP inspections in verifying that the entity is compliance with the regulations.

Chapter 10 Quiz

CHAPTER 11: TRAINING

OBJECTIVE: To become familiar with the regulatory requirements for training to ensure that the entity training program meets the requirements.

For self-study it is recommended that you take the Self-Evaluation Exam after you have completed reading the chapter. Compare your answers with the answers provided and review any areas where you did not provide the correct answers. If you have questions about the information provided or you have questions that are not covered by the material in this chapter contact the FSAP for assistance.

"Guidance for Meeting the Training Requirement" provides guidance on training requirements outline in the Select Agent Regulations.

Regulations

The regulatory requirements for training can be found in Section 15 of the Select Agent Regulations (42 CFR §73.15, 9 CFR §121.15 and 7 CFR §331.15.). The training requirements are identical in each of these regulations. For convenience §73.15 will be used in this chapter but it should be understood that the information provided refers equally to §121.15 and §331.15. Individuals that access select agents and toxins must know the requirements if they are to be compliant. The RO is responsible for ensuring that the individuals at their entity, for whom training is required, are trained in the areas specified, that they understand the training, that they receive training at least annually and that the training is documented.

Training Required

The training that must be provided is described in §73.15(a) which states,

> "An individual or entity required to register under this part must provide information and training on biosafety, security (including security awareness), and incident response to:
>
> (1) Each individual with access approval from the HHS Secretary or Administrator before that individual has such access to select agents and toxins. The training must address the particular needs of the individual, the work they will do, and the risks posed by the select agents or toxins; and
>
> (2) Each individual not approved for access to select agents and toxins by the HHS Secretary or Administrator before that individual enters areas where select agents are handled or stored."

The entity registered to possess, use and transport select agents and toxins, must provide information and training in biosafety, security and incident response. Security awareness must be part of the security training.

The regulations do not state that the training must be specific to the entity but the training will not be of value to the entity staff if they cannot connect it to entity safety, security and incident response policies and procedures. This is not to suggest that the entity cannot use training programs available from educational or other resources but an entity should ensure that training specific to the entity is also included. It may also be possible for entities to join others in the area to do join training which helps to defray costs. If the entity uses these approaches the RO should ensure that these are complemented with entity specific training.

It is important that the training program is kept current and incorporates any changes in entity policies or procedures. Anytime a new research project is planned, new facilities or equipment are added, or the entity plans to work with different agents or toxins the RO should review the training

program to confirm that it is still appropriate. Occasionally there are changes in the regulations made by the FSAP. The RO should ensure that any FSAP changes that impact the entity are incorporated into the entity training program.

Training Development

The regulations do not require the RO to develop the training program or to conduct the training but under section §73.9 (§121.9 or §331.9) the RO is required to ensure that the training is conducted and documented. The RO may personally develop and deliver the training or may delegate the training to other members of the entity. There may be a number of resources available both within the entity and outside the entity available to the RO to help with the training requirement. The entity may have a training department within the institution that can be a resource to the RO in developing and conducting training.

There are no specifications in the regulations on what is considered an acceptable training program. The entity has a wide range of options for how to set up a training program. For example, an entity could develop a slide deck presentation that covers the basics of the topics. Another approach is to require the staff to read the appropriate standard operating procedures or the appropriate plans. On line self-study training programs are also ways some entities provide training. An entity may have members of the organization give presentations. Another example might be security training by the head of security at the institution. The training may also be provided by outside experts such as someone from the community HAZMAT team or someone from the FBI Weapons of Mass Destruction regional office.

Please notice that the entity must provide "information and training". If the entity provides information on what personal protective equipment must be used before entering the BSL-3 laboratory but does not provide instruction on how to put the equipment on and take it off then the entity has only provided information and not training. Some entities will combine classroom presentations with a mentoring program. This provides both information (classroom) and training (mentoring). Some entities will ask the individual to read the biosafety manual and acknowledge that they have read it. While this provides biosafety information it is questionable as to whether effective training is provided using this method. There are multiple ways to meet the training requirements. The guiding principle is the training should provide information and training that makes it possible for entity staff to do their work in a safe manner and that ensures the security of the facilities and the agents.

Biosafety training should consist of how to work with select agents and toxins in a safe manner. Examples of the kind of training that should be provided is how to use the biosafety cabinet, what kind of personal protective equipment is required and how to use the equipment, what to do if there is an exposure, how to prepare and used disinfectants, and the specific hazards of the select agents or toxins the entity uses.

Security training should consist of information on how to protect the select agents and toxins from theft or loss. Examples are what to do if a staff member loses their key or ID badge, what to do if they encounter someone in the laboratory who is not authorized, who to notify if select agents or toxins are found missing, and what to do if a suspicious package is delivered. Examples of security awareness are how to recognize breaches in security and who to notify, what to do if a colleague is acting strangely or is threatening others, and what to do if an individual, who is not a member of the entity, is asking specific questions about security procedures.

Incident response training should consist of information on how to react to emergencies. Examples include the correct response if the fire alarm goes off, how to exit containment in an emergency, what to do if a colleague collapses in containment, where to go if there is a tornado warning and what to do if the air handling system goes down.

An entity must ensure that the training provided is appropriate for the work that the employees are performing. For example, the engineer that maintains the air handling systems would not require the same level of biosafety training as the laboratory technician who conducts animal research with Bacillus anthracis using aerosol equipment. The training that each receives should be designed to ensure that they can carry out their responsibilities without causing harm to themselves or to their fellow co-workers and the public.

The entity can meet this requirement in several ways. One way is to provide general training in safety, security and incident response which everyone would participate in and then specific training would be provided depending on the work they perform. For example, an animal technician would be provided the training on the risk presented by infected animals while an engineer would be trained on how to ensure equipment is decontaminated before conducting maintenance. Another option is for the entity to separate individuals into groups by the risk posed and provide the appropriate training to each of these groups. Some entities may require the principal investigator or the laboratory manager to be responsible for developing and conducting the training. If this is the approach used it is important that the RO ensure the training meets the requirements and is consistent across units.

Tier 1 Training

There is a special training requirement for those entities that have Tier 1 select agents and toxins. This is specified in 42 CFR §73.15(b), 9 CFR §121.15(b) and 7 CFR §331.15(b).

> "Entities with Tier 1 select agents and toxins must conduct annual insider threat awareness briefings on how to identify and report suspicious behaviors."

Any entity that has Tier 1 agents and toxins must conduct annual insider threat awareness briefings. Chapter 7 provides information on insider threat awareness briefings and should be consulted. The regulation does not state who must receive the briefings but it is implied that this would apply to those individuals who have a security risk assessment and it should be provided before they begin work with the select agents and toxins. These briefings must be documented in the individuals training record. Visitors to the laboratory would not be expected to receive this type of training because they would not have sufficient knowledge of the entity.

Who the Training Must Be Provided To

The regulations describe the individuals that must receive the training in §73.15 (a)(1) and (2), §73.15 (a)(1) and (2), §331.15 (a)(1) and (2). We will look at these separately because §73.15(a)(1), §121.15(a)(1), and §331.15(a)(1) addresses individuals with approved access and §73.15(a)(2), §121,15(a)(2), and §331.15(a)(2) addresses individuals that are not approved for access.

§73.15(a)(1), §121.15(a)(1), §331.15(a)(1)

> "(a) An individual or entity required to register under this part must provide information and training on biosafety, security (including security awareness), and incident response to:
>
> (1) Each individual with access approval from the HHS Secretary of Administrator before that individual has such access to select agents and toxins. The training must address the particular needs of the individual, the work they will do, and the risks posed by the select agents or toxins; and"

The second sentence of subparagraph (1) describes the kind of training that is required and we covered that above when we discussed the kind of training the entity must provide. The first part of subparagraph (1) states that anyone who has

received access approval from either the HHS Secretary (Director, DSAT), or the Administrator (Director, AgSAS), through the Security Risk Assessment (SRA) process to have access (able to put their hands on the select agents or toxins) must receive the required training before they are allowed to have access. The SRA was discussed in Chapter 7.

Some entities will list in their application a number of individuals who require a SRA. Some of these individuals may never place their hands on the select agents and toxins but the entity has determined that they have the potential to access the select agents. Never-the-less, if they receive approval to have access through the SRA process they must receive training in biosafety, security and incident response. It is important to emphasize that before an individual is allowed by the entity to access the select agents and toxins they must have an approved SRA and they must have received training.

Some ROs may question whether a person who has just joined the entity and has many years of laboratory experience, or may be a national leader in their field, needs to receive the required training. The answer is, if they go through the SRA process, they must receive the training. It is important to recognize that no matter how many years of laboratory experience an individual has every laboratory is different; different floor plans, different equipment, different protocols, and different policies. It is important for each new person to become aware of the features that are unique to the entity they join.

The other type of individuals who must be trained is specified in 42 CFR §73.15(a)(2), 9 CFR §121.15(a)(2), and 7 CFR §331.15(a)(2).

> "(a) An individual or entity required to register under this part must provide information and training on biosafety, security (including security awareness), and incident response to:
>
> (2) Each individual not approved for access to select agents and toxins by the HHS Secretary or Administrator before that individual enters areas where select agents or toxins are handled or stored (e.g., laboratories, growth chambers, animal rooms, greenhouses, storage areas, shipping/receiving areas, production facilities, etc.) Training for escorted personnel must be based on the risk associated with accessing areas where select agents and toxins are used and/or stored."

Prior to entry to these areas these individuals must receive training first and there must be documentation that the individual acknowledged receiving the training. The type of training they receive must be appropriate for the risk that the person is likely to encounter in the area. The training that is provided is not expected to be as extensive as it is for those that have access to the select agents and toxins. It may consist of what to do if an alarm goes off, what personal protective equipment is required and how to put it on and take it off, which areas are not to be entered and what to do if the visitor becomes ill after visiting the area. If the individual to be escorted into the area will only be there for a couple of hours, such as a FSAP inspector, the training may be very brief. If the person will spend the entire day in the area, such as a visiting scientist observing a research protocol, the training might be more extensive because the risk is potentially greater.

The RO may question whether an engineer who goes into the entity three for four times a year to check the air handling systems needs to receive training each time and the answer is, no, recurring visitors must receive training once per calendar year. There must be documentation that they acknowledge they have received and understood the training.

It is important for the RO to ensure that everyone who is escorted into an area where there are select agents and toxins, whether they are being used or just in storage, has acknowledge receiving training

before entering the area. It is recommended that the RO periodically compare the containment access records with the training records to ensure that everyone who enters the containment area has received the training.

RO Training

The Federal Select Agent Program recognizes that the responsibilities of an RO require a broad spectrum of knowledge, skills, and abilities. The RO is evaluated by the Federal Select Agent Program on how they conduct their responsibilities and how well their entity maintains compliance with the regulations. This does not mean that the RO should not document any training they receive in biosafety, security and incident response, but only that specific documentation is not a requirement under the current regulations. The FSAP conducts workshops annually on the select agent regulations and ROs are encouraged to take advantage of these training events and others that are available.

Multiple use areas

Laboratories that are multiuse areas present a special situation that the RO must address. An example of a multiuse laboratory is one that is used for select agents and toxins but is also used as a TB or HIV diagnostic laboratory. The simple approach is to require all individuals who enter the laboratory to have an approved security risk assessment and ensure they are provided the required information and training.

Another approach is to document those times when select agents and toxins are stored and used in the laboratory and ensure that anyone who enters the laboratory during that time period has been provided the specified training.

Frequency of Training

The frequency of training is specified in §73.15(c), §121.15(c), and §331.15(c).

> "Refresher training must be provided annually for individuals with access approval from the HHS Secretary or Administrator or at such time as the registered individual or entity significantly amends its security, incident response, or biosafety plans."

Training must be provided to everyone at the entity who has an approved SRA at least annually. If the entity makes significant changes to the biosafety, security or incident response plans then the entity needs to update their training programs and provide the training to the staff. Some examples of situations that may prompt a need for refresher training are:

- Renovation of the research building resulting in changes to biosafety, security and incident response policies and procedures.
- A principal investigator begins a new project that has select agents never used before and different protocols are implemented.
- The security system has been upgraded.
- The Federal Select Agent Program has amended the Select Agent Regulations.
- Changes to the building have changed emergency access routes.

Refresher training does not necessarily need to be as extensive as the training a person receives when they first join the entity. Refresher training should consist of at least an overview of biosafety, security and incident response but this also presents an opportunity to focus on specific topics in biosafety, security and incident response. If there have been several security breaches during the year the RO may want to focus refresher training on the causes

for those incidents. If there have been several incidents of releases of select agents the RO may focus the biosafety training on the causes of the releases. These are just some examples of the kinds of refresher training topics that the RO could include.

Refresher training is required to be provided annually. The Federal Select Agent Program recommends that the time frame should be closer to a 12-month interval between annual refresher training events unless there is a reason for the training to occur sooner, such as significant alteration to an entity's plan or procedure. The refresher training may incorporate biosafety, security and incident response into one training event or may divide these subjects into different training events.

Drills and exercises are required by the regulations to test the biosafety, security and incident response plan and this is covered in Chapter 12. Drills and exercises are excellent opportunities for a training experience. In conducting an exercise on what to do when a person collapses in the laboratory the individuals that participate in the exercise learn about biosafety and emergency response procedures. This satisfies the requirement to conduct a biosafety and incident response drill but it may also help to satisfy part of the refresher training requirement for those that participate.

Training Records

In addition to ensuring that training is provided in accordance with the requirements that have been discussed above the RO must also ensure that there are records of the training. This requirement is stated in §72.15(d), §121.15(d), and §331.15(d):

> "The Responsible Official must ensure a record of the training provided to each individual with access to select agents and toxins and each escorted individual (e.g., laboratory workers, visitors, etc.) is maintained. The record must include the name of the individual, the date of the training, a description of the training provided, and the means used to verify that the employee understood the training."

For each individual listed as having access to select agents and toxins there must be a record that the individual has received the required training. The RO should establish a record on each individual at the time the person receives the initial training and then record when the individual receives refresher training. The record must be maintained for a period of at least three years, even if the individual leaves the entity before the end of three years. There is no specified way to record the training other than the record must contain the name of the individual, the date they receive training, a description of the training provided and the means used to verify that the individual understood the training. Some entities will establish a file on each individual that includes all training the individual receives, not just select agent training. Some entities will establish a checklist of all the training the person is required to take and the person providing the training signs the checklist when training has been provided.

There must be a means for verifying that the individual understands the training that they are provided. Some entities will give an individual a test to determine if they understood the material or ask that the individual sign the record that they understood the training. During an inspection by the FSAP the inspector may interview staff members at random about their knowledge of biosafety, security and incident response to determine if they have received and understood the training.

Training records must also be maintained for three years on anyone who does not have an approved SRA but goes into an area where there are select agents and toxins. The RO must be able to produce a record that individuals who are escorted into laboratories with select agents and toxins have received instructions and have signed that they received and understood the instructions. Most entities will have a one or two page document

listing the name of the individual who enter the area, the information and training they were provided and the signature of the individual verifying that they received the training.

In summary, the RO is responsible for ensuring that everyone who has access to select agents and toxins and everyone who enters an area where select agents are stored and used is provided training in biosafety, security and incident response and that the training is documented. The way this is accomplished is up to the entity but it is important to ensure that the staff operate in a safe manner and that the select agents and toxins are kept secure.

Chapter 11 Quiz

CHAPTER 12: DRILLS AND EXERCISES

OBJECTIVE: To become familiar with the requirement to conduct security, safety and incident response drills or exercises.

For self-study it is recommended that you take the Self-Evaluation Exam after you have completed reading the chapter. Compare your answers with the answers provided and review any areas where you did not provide the correct answers. If you have questions about the information provided or you have questions that are not covered by the material in this chapter contact the FSAP for assistance.

Introduction

Registered entities are required to conduct drills and/or exercises at least annually that test the entity's biosafety, security and incident response plans. This is a requirement listed in sections 11 (Security), 12 (Biosafety), and 14 (Incident Response) of the regulations (42 CFR Part 73, 9 CFR Part 121 and 7 CFR Part 331). The terms, "drills" and "exercises" are used interchangeably to mean conducting an activity that tests the response to a potential event. The regulations do not specify that the drills and exercises must be documented but the RO may be asked by FSAP inspectors to provide evidence the entity has performed activities to ensure biosafety, incident response and security plans are adequate.

The purpose of requiring the drills/exercises is to confirm that the biosafety, security and incident response plans provide the necessary policies and procedures to ensure the level of biosafety, security and incident response determined by the risk assessment. Drills/exercises provide opportunities to identify gaps and to detect flaws in the plans. Drills/exercises can also be excellent tools for training the entity staff on biosafety, security and incident response.

The regulations do not provide instructions on what kind of drills/exercises should be conducted or how they should be conducted. Some entities hire outside organizations to assist in conducting drills, some entities develop their own programs and some entities will combine with other entities or local and state groups to conduct drills. There does not necessarily need to be a separate drill for biosafety, security and incident response. Some drills/exercises can be linked together such as a combined security and incident response. However the entity determines to meet the requirement the participants selected for the drill/exercise is an important consideration. A biosafety drill/exercise should involve laboratory staff and biosafety personnel but may also involve engineering staff or individuals from outside the organization. An incident response drill/exercise may be structured to involve community emergency responders or state emergency preparedness personnel. A security drill/exercise should involve the institution's security personnel but may also include the local police or the Federal Bureau of Investigation Weapons of Mass Destruction Office. The drill/exercise can be a table top event or a more elaborate physical activity. One of the best times to conduct the annual drills/exercises is when the laboratory is shut down for maintenance. The RO may also wish to take advantage of the opportunity to use actual incidents to meet the drill/exercise requirement. This can be done by reviewing the responses to the incident after the event to determine if the procedures for dealing with the incident were adequate or are improvements needed.

Listed below are examples of drills/exercises. It is not a comprehensive list but only examples of the kind of drills/exercises that can be done. The entity facilities, agents possessed, work activities and plans should be considered when determining the types of drills/exercises to conduct.

Examples of Drills/Exercises

Biosafety:

- Simulate a spill of infectious materials in the laboratory and test the response by personnel using the established instructions for dealing with a spill.
- Simulate the collapse of a person in the laboratory and test how people respond, what communication is conducted, how the person is removed from the laboratory. This can be done as a collapse during business hours and as one that occurs after business hours.
- Simulate a power failure that results in main and auxiliary power sources failure.
- Simulate a sudden release of large amounts of steam from the autoclave or the falling of a CO_2 tank.
- Simulate failure of PPE such as a tear in a glove, failure of the PAPR, or spill of agents or toxin on a scrub suit.
- Simulate release of infected animals. This can be with small animals and with large animals depending on the type the entity works with.
- Simulate receipt of a package with select agents in the receiving area that is found to be leaking.
- Simulating exposure of a worker to an agent is a good way to test the medical surveillance protocols.

Security:

- Simulate a break-in of the laboratory and note how soon security responds.
- Simulate discovery of an unauthorized individual in containment.
- Simulate a bomb threat or a threat to laboratory personnel.
- Simulate a situation where a staff member becomes irrational and creates a disruption or produces a weapon.
- Simulate an explosion in the containment that results in access to the select agent stored area.

Incident Response:

- Simulate any of the natural hazards appropriate for the area such as tornado, hurricane, flood, severe weather, etc.
- Simulate complete disruption of all normal communication systems.

Chapter 12 Quiz

CHAPTER 13: INSPECTIONS

OBJECTIVE: To become familiar with how the Federal Select Agent Program (FSAP) conducts entity inspections and how to prepare for an inspection at your entity.

For self-study it is recommended that you take the Self-Evaluation Exam after you have completed reading the chapter. Compare your answers with the answers provided and review any areas where you did not provide the correct answers. If you have questions about the information provided or you have questions that are not covered by the material in this chapter contact the FSAP for assistance.

Informational video about the select agent inspection program is provided to ensure compliance to the select agent regulations. The video describes how to prepare for an inspection and what transpires during and after an inspection. It can also be helpful to have those at the entity who will be involved in the inspection to review this video so they have some understanding of what to expect.

Introduction

The Select Agent Regulations states the following:

> (a) Without prior notification, FSAP is allowed to inspect any regulated site and copy any records.
>
> (b) Prior to issuing a certificate of registration to an individual or entity, FSAP is allowed to inspect and evaluate the premises and records to ensure compliance with the Select Agent Regulations.

The entity inspection is the primary means used by the FSAP to verify that the entity is in compliance with the Select Agent Regulations. The inspection can also be viewed as an opportunity for the entity to receive a review of the facilities and the biosafety and biosecurity practices of the entity by outside experts and to receive input on improvements. In this sense, the inspection can be a valuable learning experience for the entity.

Inspections

Inspections may be conducted by one or more inspectors from the FSAP and the inspection will normally be at least two days in duration but the number of inspectors and the duration will depend on the size and complexity of the entity's select agent program. There are multiple variations of the inspection event and the purpose of the inspection is a factor in how the inspection is conducted. The types of FSAP inspections are:

- **New registration or registration renewal inspection.** This is the most common type of inspection and the one that is usually the most comprehensive. For entities that only have a few laboratories, the inspection will usually be two days in duration and conducted by two inspectors. For larger institutions, the inspection can be as long as three weeks and involve up to 20 inspectors. These types of inspection are usually conducted every three years.

- **Verification/Compliance inspection.** The purpose of the inspection is to verify that the entity has resolved the deficiencies noted in a previous inspection. It is not uncommon for these inspections to be unannounced. The inspection is usually focused on specific areas such as security, biosafety or on previously noted deficiencies and these inspections tend to not be as comprehensive as a renewal inspection. This type of inspection usually occurs within 12 – 18 months after the registration inspection but if there are serious deficiencies there could be multiple inspections over a short time.

- **Registration amendment inspection.** If there are major changes in an entity's registration such as the addition of new agents, new laboratories, or changes in work objectives, the FSAP will most likely conduct an inspection to verify that the changes are in compliance with the requirements of the select agent regulations.

- **Inspection for cause.** In the case where there has been a loss of select agents or toxins, an exposure requiring treatment or serious uncorrected deficiencies, the FSAP will usually conduct an inspection which will be unannounced. If the FSAP determines that significant violations have occurred, the entity may also be referred to the Health and Human Services Office of Inspector General, the USDA Investigative Enforcement Service or the Federal Bureau of Investigation.

- **Multiple agency inspection.** In all of the above types of inspections, there may be other agencies besides the DSAT and AgSAS involved. The Department of Defense Office of Inspector General, the Department of Homeland Security, the Department of Transportation and others may participate in a FSAP inspection. Even though these agencies do not have authority under the Select Agent Regulations, the FSAP and other federal agencies have agreed to coordinate inspections when possible to avoid an undue burden on entities.

Inspection Process

The process for a regular announced inspection is best viewed as a three phase process. The three phases are the pre-inspection, inspection and post-inspection. Each of these phases is described in detail below.

- **Pre-Inspection Phase** – The pre-inspection phase is the phase in which the RO is notified of a pending inspection and begins to prepare for the inspection event. The RO should provide any information requested by the FSAP, inquire about the inspection process, notify entity personnel of the pending event and prepare the documentation that will be examined by the inspectors. Inspection checklists, which are used by the inspectors can be helpful for the RO to review in preparation for the inspection.

- **Inspection Phase** – This is the onsite inspection phase where inspectors arrive at the site and begin the inspection. The typical inspection constitutes the following activities:

  - Introductions by inspectors and entity personnel

  - Description of the inspection process by the inspectors and discussion of the inspection schedule. Inspectors will need a room during the duration of the inspection where documents can be examined and interviews conducted. The room should be lockable to allow inspectors to secure materials while conducting a review of the facilities.

  - Presentation by the principal investigators or laboratory managers on the select agent and toxin related activities that are conducted at the entity. This is not expected to be a lengthy presentation but just enough to give the inspectors a sense of work being performed with the select agents and toxins at the entity.

  - Physical examination of the laboratories and the laboratory supporting areas (HVAC systems, liquid decontamination systems, waste handling systems, physical security systems, engineering controls). This can be a lengthy process depending on the number and complexity of laboratories. Access to the laboratories is required and inspectors should be notified prior to the inspection of any access requirements such as personal protective equipment and immunizations. During this phase an inventory, either spot check or complete inventory is usually conducted.

- Examination of records and documentation. This includes a review of the current biosafety, security and incident response plans, equipment maintenance records, commissioning or annual facility verification documents, access records, training programs and records, transfer records, internal audit documents, and where applicable, reports of theft, loss and release, incident reports, and description of the entity occupational health program and Institutional Biosafety Committee minutes.

- Interviews are conducted throughout the inspection process. This will involve interviews with security and safety personnel, laboratory staff, researchers, and engineers.

- At the conclusion of the inspection, the inspectors will provide a briefing of the primary findings during the inspection. This will not be a complete listing of all observations that will be included in the written report but will provide the RO an idea of the observations that will be included. This is also an opportunity for the RO and other entity staff to ask questions of the inspectors.

- **Post-inspection Phase** – Within 2 – 3 weeks, a written report of the findings during the inspection will be provided to the RO. The report will list the observations made by the inspectors including the description of how the regulatory requirement was not met. Before the report is sent to the RO, the report is reviewed by FSAP management to ensure accuracy. The RO generally has 14 calendar days to respond to the report providing detailed responses and documentation to support that the deficiency has been corrected. If the deficiency cannot be corrected within the 14 days, the RO should provide a detailed plan for correction of the deficiency including milestones. If the responses are not adequate, the RO will receive additional requests for information. During this phase, the RO should contact the inspectors if there are any questions about the observations. This is important as it saves time and effort by the RO and the inspectors if there is a clear understanding of the issues.

After the FSAP has determined that all of the deficiencies have been adequately addressed, the RO will receive a letter stating that the inspection has been closed and no additional information is required.

The inspection described in this chapter is a routine scheduled type of inspection. It should be understood that while the inspection process is as standardized as possible every entity is different and no two inspections are identical.

Chapter 13 Quiz

CHAPTER 14: FACILITIES: COMMISSIONING AND VERIFICATION

OBJECTIVE: To gain an understanding of expectations of the entity in regards to the facilities where select agents and toxins are stored and used and how these facilities are evaluated to ensure they provide adequate safety for the laboratory staff and the public.

For self-study it is recommended that you take the exam for Chapter 14 that you will find in Appendix AK after you have completed reading the chapter. Compare your answers with the answers provided and review any areas where you did not provide the correct answers. If you have questions about the information provided or you have questions that are not covered by the material in this chapter contact the FSAP for assistance.

The FSAP has expertise in the evaluation of containment facilities and this is part of the inspection verification process. The FSAP cannot provide pre-inspection or pre-construction consultation. There are resources that the RO may wish to consider and firms that specialize in containment construction and consultation.

Introduction

Inward directional airflow is a secondary barrier to minimize the exposure of laboratorians to potentially infectious aerosols. The BMBL, 5th ed., makes the following recommendations regarding the design of BSL-3 and ABSL-3 laboratory ventilation systems:

- BSL-3 D9: "The laboratory shall be designed such that under failure conditions the airflow will not be reversed."

- ABSL-3 D6: "The ABSL-3 animal facility shall be designed such that under failure conditions the airflow will not be reversed."

The BMBL, 5th ed., also makes the following recommendations regarding BSL-3/ABSL-3 general facility verification, as follows:

- BSL-3 D15: "The BSL-3 facility design, operational parameters and procedures must be verified and documented prior to operation. Facilities must be re-verified and documented at least annually."

- ABSL-3 D14. "The ABSL-3 facility design and operational procedures must be documented. The facilities must be tested to verify that the design and operational parameters have been met prior to use. Facilities should be re-verified at least annually against these procedures as modified by operational experience."

The information provided in this chapter focuses on BSL-3 and ABSL-3 but many of the comments may apply to BSL-4 and ABSL-4 containment facilities. There are however additional requirements for level 4 containment that this chapter does not address. It should also be recognized that there are many variations of level 3 containment and the type of verification and monitoring should be that which is appropriate for the particular type of containment.

Engineering Support

The engineering support components of containment facilities are a major contributor to the safe operation of biological laboratories. Involving the institution engineering staff in learning about the support components and educating the engineering staff on the needs of the laboratory is an activity that can pay dividends for the biosafety program. There are challenges in doing this. In a large entity there is usually a group of engineers with different talents. It is helpful if

a few dedicated engineers can be identified who have the necessary expertise and the interest in supporting the containment facilities. In some cases there may be reluctance on the part of engineers to get involved in work that could expose them to infectious disease agents. This is where educating the engineers on the hazards and how to avoid them and listening to and addressing their concerns is important. It is equally critical to involve the engineers in decisions about the containment facilities, so that the risk of inadvertent releases of select agents or toxins can be more effectively managed. For small facilities the challenge may be in identifying engineering expertise that has the time and interest in supporting the laboratory. Level 3 containment facilities are unique and it is important for the engineering support staff to learn the special requirements of these types of facilities. If the engineering support is contracted it is still important that there be a facility engineer who can monitor the contractor activities. Contractors too must have the special expertise required for level 3 containment facilities maintenance.

Commissioning

No high or maximum containment facility should be put into operation until it has gone through the commissioning process. This applies to new facilities as well as facilities that have undergone considerable renovation. Commissioning is a very broad term for a systematic process of verifying and documenting that all technical facility systems perform as designed and meet operational needs. The building systems tested during commissioning include HVAC, plumbing, lighting, electrical, etc., and depend upon the complexity of the design. The components of commissioning which are considered minimal requirements are listed below as HVAC and general facility verification. HVAC verification tests should be performed by individuals who have experience with HVAC systems for containment facilities and have the expertise necessary to ensure that the containment facility is designed and operates to avoid exposure of personnel outside of containment. Commissioning is often performed by companies experienced in the process especially if it is a maximum containment facility (BSL-4/ABSL-4). Some entities may have their own in house expertise. Regardless of who conducts the commissioning it is important for the RO to confirm that the work performed is in accordance with the requirements that are listed below. Commissioning is expected to involve confirming that the HVAC systems functions to maintain secondary containment under failure conditions. The failure conditions include:

- Mechanical failure of exhaust fan or fan component(s):
  - If redundant fans are present, the ability to transition to the alternate fan without reversal of air flow from potentially contaminated laboratory space into "clean" areas surrounding the laboratory must be verified.
  - If no redundancy is present in the laboratory HVAC system, the capacity to transition from sustained inward air flow into the laboratory to a "static" condition, i.e., no air flow out of the laboratory must be confirmed.
- Simultaneous power failure supporting supply and exhaust fan components:
  - If emergency power supply is available for the laboratory HVAC system, the ability to transition from "normal" power to the backup system without a reversal of air flow from the laboratory should be confirmed.
  - If no backup power supply is available, the ability of the HAVC system to transition to a "static" condition, i.e., no outward air flow, should be confirmed.
- Return from power failure to "normal" operating conditions:
  - If emergency power supply is available, the

ability to transition from backup power to normal power without a reversal of airflow from the laboratory spaces to clean areas surrounding the laboratory should be confirmed.

- If no backup power supply is available, the ability of the HVAC system to return to normal operating conditions, without a reversal of air flow from laboratory spaces to clean areas surrounding the laboratory should be confirmed.

Testing must demonstrate that under exhaust fan or normal power failure conditions, or during normal power start-up, there is no reversal of air which originates within the laboratory or vivarium that travels to outside the containment boundary. The containment anteroom is considered to be within the containment boundary. A positive pressure excursion is not necessarily an airflow reversal; if a brief, weak positive pressure excursion is noted, a repeat test should be performed with airflow observation using an airflow indicator such as a smoke stick, or dry ice in a container of water at the base of the closed laboratory door to confirm whether airflow reversal is occurring. If there are questions about this process and what is considered acceptable contact the FSAP.

In addition to HVAC verification the following are the initial and annual minimum facility verification requirements for BSL-3 and ABSL-3 containment laboratories:

- The means of detecting air flow (tell tale, magnehelic or digital gauge, Baulin-Tube®, etc.) has been confirmed to accurately reflect observed air flow. It is recommended, but not required, that digital or magnehelic gauges be calibrated annually.

- Inward directional airflow has been confirmed by observation for the containment rooms. The use of smoke sticks can be helpful with confirming airflow.

- Decontamination systems (autoclave, room decontamination systems, digesters, liquid effluent systems, etc.) have been confirmed to operate within specifications. A means of validating that the decontamination systems are effective is recommended.

- All alarms (fire, air flow, security, air supply) have been checked and are functioning within specifications.

- HVAC HEPA filters, if present, have been certified.

- Exhaust fan motors have been checked and routine maintenance conducted. This may include belt inspection and replacement if needed, bearing wear checks, etc.

- Containment rooms have been checked for unsealed penetrations, cracks, breaks, etc. and these have been repaired if present.

- All biological safety cabinets have been certified.

- Seals on centrifuges, Class III cabinets, gloves on Class III cabinets, etc., have been checked and replaced if cracked, worn or have breaks.

- Drench showers, eye wash stations, and hands free sinks have been checked to confirm they are operating properly.

- If the entity has a building automation system the system should be tested to ensure that it is accurately monitoring as specified and that out of range alarms are functioning.

Some older facilities may have never been commissioned, or if they were commissioned the documentation cannot be found. If this is the case then it is recommended that the entity conduct the testing that is listed above and document this testing in conjunction with initial registration with the FSAP.

Initial and Annual Facility Verification

Once commissioning of the containment facilities has been performed and approval from the FSAP has been obtained it is not necessary to conduct HVAC failure testing provided there have been no major changes made to the HVAC system and no major problems noted with HVAC failure. Examples of major changes to the HVAC system which may require re-verification of HVAC design functionality under failure conditions include replacement of exhaust or supply fans, replacement of ductwork valves, or dampers, replacement or repair of HVAC system control wiring, building automation system logic programming changes, structural changes to the containment rooms or addition or removal of hard-ducted safety cabinets or fume hoods. Frequent failures of the HVAC system, supply-exhaust interlocking system failure, problems in establishing or maintaining air balance, reversal of air flow under normal conditions, failure of HVAC alarms or problems with hard ducted safety equipment are additional reasons to consider conducting HVAC failure conditions testing.

The BMBL, 5th ed., states that annual verification must be conducted. Unless the entity can provide justification for not performing annual verification the verification should be done. Annual verification has the advantages of allowing for cleaning and decontamination of the laboratory, and routine maintenance and checking or replacement of equipment. It also presents an opportunity to retrain staff and conduct drills and exercises. It has been argued that entities with building automation systems are constantly monitoring the containment parameters and therefore never need to be shut down. Never-the-less for reasons already stated it is recommended that the containment facility be periodically shut down.

HVAC failure conditions testing should never be performed when the laboratory is operational. The laboratory should always be decontaminated and verified that it is clean before conducting any HVAC testing. It is also important that the engineering, or facility maintenance, staff do not conduct maintenance on exhaust air systems, duct work, liquid decontamination, HEPA filters, safety cabinets or other equipment potentially exposed to infectious disease agents without first consulting with the RO and biosafety officials. If emergency situations require maintenance on containment systems all precautions should be instituted to minimize potential exposure of personnel to infectious disease agents.

Documentation

It is important to document commissioning and verification activities. This should include who conducted the commissioning and verification, what parameters were checked, what deficiencies were found and when and how the deficiencies were corrected. If there are incidents that involve HVAC failure, alarm failure, equipment failure or similar types of events these should be documented as to when the incident occurred and what was done to correct the problem. If there is an exposure, or potential exposure, of personnel this should be reported to the FSAP using APHIS/CDC Form 3. If building automation systems are used there should be records maintained of the recordings and any incidents that occur. It is also recommended that any routine checks of the operation of the system be documented. All documents should be maintained for at least three years. It is recommended that any commissioning documentation be retained for as long as the containment area is in operation. Commissioning, verification, and maintenance records are usually maintained by the entity's engineering, or facilities management office. If this is the case it is recommended that the RO periodically conduct a review of these documents to ensure that the required records are complete and up to date. FSAP inspectors may request copies of such documents during an inspection if there have been new spaces added to the registration, construction or repair has been performed in the registered space or there have been reports of failures.

Chapter 14 Quiz

APPENDIX A: THREE YEAR CYCLE OF RO TASKS

The Three Year Cycle of Events is a listing of the events that can occur over a three year time span from initial registration to registration renewal. It does not include all possible events and there will be variation of events among entities. The intent of the table below is to give the Responsible Official (RO) an overview of the activities that can occur prior to and during registration and then activities after registration during the three year registration cycle. This is hoped to provide the RO with a reminder of checklist of tasks associated with managing their entity select agent program. Please refer to the documents in this manual and the FSAP web site for additional details.

Note: The shaded areas are tasks performed by the FSAP.

Event	Description of Event	Comment
1.0	Entity identifies need to register with FSAP	This decision should involve the key members of the organization and after review of the regulations. Contact the FSAP for questions about registration and the regulations. See Chapter 3.
2.0	Entity selection of individual to be RThe entity may also at this point designate an alternate RO or delay this to later. Consideration should be given to the RO duties and responsibilities as specified in the regulations. See also Chapter 2.	
3.0	Community outreach	Depending on the work to be performed and the entity's policies and philosophy it can sometimes be helpful to proactively reach out to local community leaders to address community fears and concerns. This may especially be important if a maximum containment facility is the issue.
4.0	Conduct review of the facilities where BSAT will be stored and used	Facilities should be appropriate for the agents and work to be performed and operational ready. Refer to the Biosafety in Microbiological and Biomedical Laboratories, 5th Edition and the FSAP for guidance. Please note that the facilities should be ready for operation.
4.1	Conduct biosafety risk assessment and develop biosafety plan	The plan should be specific to the select agents and toxins that will be possessed, used or transferred and should complement, not conflict with, any organization wide plans.

Event	Description of Event	Comment
4.2	Conduct security risk assessment and develop security plan	The plan should be specific to the BSAT that will be possessed, used or transferred and should complement, not conflict with any organization wide plans. The FBI WMD regional office can be helpful in assisting with security risk assessments. There is also guidance documents provided on the FSAP web site. It is also important to put additional security in place if Tier 1 agents are used.
4.4	Conduct hazard threat assessment and develop incident response plan	The plan should be specific to the BSAT that will be possessed, used and transferred and should be consistent with any organization wide plans. Entity should contact and involve local emergency responders. See Chapter 8.
4.5	Develop training program and begin staff training.	Refer to training guidance provided on FSAP website. See Chapter 11.
5.0	RO prepares the application (APHIS/CDC Form 1 and submits to FSAP	Engaging members of the entity in preparation of the application can be helpful in building requirements knowledge among the staff and insuring that all requirements are covered. Refer to Chapter 3.
6.0	FSAP receives application and sends acknowledgement with DOJ numbers for staff identified as needing access	Approximate time to receive DOJ numbers is 5 – 10 business days.
6.1	FSAP assigns File Manager to entity	File Manager is the point of contact and should contact the RO within 5 – 10 business days.
7.0	Entity personnel submit FD-961 and finger prints to Criminal Justice Information Services (CJIS)	To avoid delay in processing all information should be provided. RO is expected to sign forms before they are sent to CJIS. Processing takes 30 – 50 calendar days to complete
7.1	RO and staff member receive approval or disapproval from FSAP of Security Risk Assessment	Restricted individuals can appeal decision by following instructions on notification.
7.2	Training on security, safety and incident response conducted by entity of all personnel involved in entity select agent program.	See Chapter 11.
8.0	RO is contacted by FSAP to arrange inspection	Inspection is generally scheduled 60 – 90 days in advance but may be unannounced.
9.0	RO prepares for FSAP inspection	RO can use checklists found in this manual site as an aid in evaluating the entity for compliance with the regulations. There is a video of the inspection process on the FSAP website that can be helpful in what to expect during an inspection.

Event	Description of Event	Comment
10.0	FSAP sends RO notice of inspection	Notice of inspection is general sent to the entity as least 30-45 days in advance of the inspection.
10.1	RO provides entry requirements and other required information to the FSAP.	Information on security, immunization, and personal protective equipment requirements should be sent to the FSAP prior to the inspection. Additional documentation may also be required such as biosafety, security and incident response plans.
11.0	FSAP inspectors arrive to conduct inspection	Inspections are generally 2-3 days in length and involve 2 -3 inspectors. This in influenced by the size and complexity of the entity.
12.0	FSAP sends inspection report to RThe inspection report will be sent within 14 – 28 calendar days after the inspection.	
13.0	RO receives report and prepares responses to any noted deficiencies	The RO has 14 calendar days to respond to the inspection report. If inadequate responses are provided additional requests from the FSAP for information will be requested.
14.0	FSAP sends notice that all deficiencies have been addressed.	The resolution of inspection deficiencies is not approval to possess select agents and toxins.
15.0	FSAP sends certificate of registration to the RThe certificate is valid for a period of 3 years and conveys approval to possess select agents and toxins.	
16.0	Entity acquires BSAT they are registered for using the APHIS/CDC Form 2	All transfers of select agents and toxins at registered levels must be approved prior to shipment.
16.1	RO submits amendments to registration anytime there are changes to the application	APHIS/CDC Form 1 is used for amendments. See Chapter 3 for additional information and the FSAP web site.
16.2	RO submits APHIS/CDC Form 3 anytime there is a theft, loss or release of a select agent or toxin	See FSAP web site for forms.
16.3	RO ensures that annual refresher training is conducted for SRA approved staff.	Training is in biosafety, security and incident response. Also threat awareness briefings are required if entity possesses Tier 1 agents.
16.4	RO submits APHIS/CDC Form 4 if select agents or toxins are identified	Select agents and toxins for which the entity is not registered must be transferred or destroyed.
16.5	RO conducts annual inspections. This includes inventory audits to ensure that the inventory is current and accurate.	Inspection checklists provided in Appendix M can be used to develop the internal inspection process.

Event	Description of Event	Comment
16.6	RO ensures that plans (biosafety, security and incident response) must be reviewed annually and revised as necessary and reviewed and revised as necessary after drills and exercises. Staff must be retrained if there are significant changes to the plans.	Drills and exercises can be done throughout the year.
16.7	RO reviews access records	Access records should be compared with the current list of SRA cleared individuals.
16.8	RO ensure training is provided to escorted individuals with access to registered areas	Training must be documented and provided to any individuals not SRA cleared who enter registered areas.
16.9	RO ensures facilities and equipment receive annual maintenance, certification, etc.	Records must be maintained for a minimum of three years.
17.0	Year two is a repeat of Event 16.0 – 16.9	Announced or unannounced inspections may occur at any time.
18.0	Year three is a repeat of Event 16.0 – 16.9	Announced or unannounced inspections may occur at any time.
19.0	RO reviews list of staff with SRA	The SRA expires after three years the RO should identify those individuals with expiring SRA at least 90 days prior to expiration and submit FD-961 to FBI. Fingerprints are not normally required for renewal of SRA.
20.0	FSAP contacts RO to schedule renewal inspection	The RO will be contacted approximately 5 – 6 months before the registration is scheduled to expire with inspection scheduled 3-4 months in advance.
20.1	FSAP sends notice of renewal inspection	The notice will be sent to the RO in approximately 45 days in advance of the inspection. RO may be requested to provide updated biosafety, security and incident response plans (occupational health plan for Tier 1 agents).
20.2	RO ensures that all records are complete and up to date.	Having all records, plans and other associated documents ready for inspectors is helpful in the inspection process.
20.3	FSAP conducts inspection of entity	This is a comprehensive review of the entity.
20.4	RO receives report of inspection with list of any deficiencies	Entity has 14 calendar days to respond. If deficiency will take longer than 14 days to resolve RO should ensure that the response provides plans to resolve deficiency along with timelines.
20.5	RO receives renewal certification	Renewal is valid for another three years.

Centers for Disease Control and Prevention
Division of Select Agents and Toxins

Animal and Plant Health Inspection Service (APHIS)
Agriculture Select Agent Program