

Department of Health and Human Services

**OFFICE OF
INSPECTOR GENERAL**

**THE FOOD AND DRUG ADMINISTRATION
GENERALLY COMPLIED WITH FEDERAL
REQUIREMENTS FOR THE PREPARATION
AND RECEIPT OF SELECT AGENT
SHIPMENTS**

Notice: Location information was redacted in this audit report.

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Office of Inspector General

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Report in Brief

Date: June 2019

Report No. A-03-16-00354

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES
OFFICE OF INSPECTOR GENERAL



Why OIG Did This Review

The Food and Drug Administration (FDA) is one of several Federal agencies that ship and receive select agents. Select agents are biological agents or toxins that HHS and the Department of Agriculture have determined pose a threat to humans, animals, plants, or the environment. In 2015, another Federal agency found that one of its facilities had inadvertently shipped live *Bacillus anthracis*, a select agent which causes the deadly disease anthrax, to 194 laboratories in the United States and other countries. In response to these events, we initiated a review of the policies, procedures, and protocols FDA implemented to ensure the safe shipment of select agents to and from its laboratories.

Our objective was to determine whether FDA has designed and put in place controls to ensure that select agent shipments are prepared and received in accordance with Federal regulations and related supporting laboratory guidance and instruction.

How OIG Did This Review

We reviewed eight select agent shipments either sent or received by one of FDA's 11 registered entities from October 1, 2013, through September 30, 2015. We also requested documentation of all inactivated select agents shipped and received during the same period. We reviewed relevant FDA policies, training documentation, and inactivations for compliance with Federal requirements and guidance.

The Food and Drug Administration Generally Complied With Federal Requirements for the Preparation and Receipt of Select Agent Shipments

What OIG Found

Generally, FDA has designed and put in place controls to ensure that select agent shipments are prepared and received in accordance with Federal regulations and related supporting laboratory guidance and instruction. However, 8 of FDA's 11 registered entities' security plans did not include certain procedures for notifying the Federal Select Agent Program (FSAP) if a select agent shipment is not received within 48 hours after the expected delivery time or a select agent shipment receives damage to the extent that a select agent release may have occurred, and none of FDA's registered entities' security plans included certain procedures for notifying FSAP if an authorization for a select agent transfer expires or becomes void before the shipment is completed. In addition, we found that FDA's registered entities did not always maintain required select agent training documentation and did not have sufficient policies to ensure compliance with all new requirements for shipping select agents that have undergone inactivation.

What OIG Recommends and FDA Comments

We recommend that FDA update its registered entities' security plans to include procedures for notifying FSAP if a select agent (1) shipment is not received within 48 hours after the expected time of delivery, (2) package is received damaged to the extent that a release of the select agent may have occurred, (3) shipment will not be completed within 30 calendar days after transfer authorization issuance, or (4) transfer authorization becomes void because the facts supporting the authorization changed. We also made recommendations regarding FDA's select agent training documentation and policies for shipping inactivated select agents.

In written comments on our draft report, FDA concurred with our recommendations and stated that it has taken actions to implement them. FDA indicated that it has developed a standardized template for the Select Agent Security Plan used by the Office of Regulatory Affairs and FDA Centers that participate in FSAP that addresses all of our recommendations. FDA also stated that it has revised its policies to address all of the recommendations. Finally, FDA provided technical comments on our draft report that we have addressed in this report as appropriate.

Notice: Location information was redacted in this audit report.

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INTRODUCTION

WHY WE DID THIS REVIEW

The Food and Drug Administration (FDA) is one of several Federal agencies that ship and receive select agents. In 2015, another Federal agency found that one of its facilities had inadvertently shipped live *Bacillus anthracis*, a select agent that causes the deadly disease anthrax, to multiple contract laboratories.¹ An investigation found that 194 facilities in the United States and other countries received live spores from samples that originated at the facility and that the process it used to inactivate *Bacillus anthracis* with radiation was not always effective.

In response to these events, we initiated reviews of the policies, procedures, and protocols implemented by two of the Department of Health and Human Services' (HHS's) divisions, the National Institutes of Health and FDA, to ensure the safe shipment of select agents to and from their laboratories. This report details the results of our review of the select agent shipment controls at FDA.

Appendix B contains a list of related Office of Inspector General reports.

OBJECTIVE

Our objective was to determine whether FDA has designed and put in place controls to ensure that select agent shipments are prepared and received in accordance with Federal regulations and related supporting laboratory guidance and instruction.

BACKGROUND

Select Agents

Select agents are biological agents or toxins that HHS and the Department of Agriculture (USDA) have determined pose a threat to humans, animals, plants, or the environment. Regardless of its origin (naturally occurring, engineered, or synthesized), any microorganism or toxin capable of harming living organisms or the environment can be classified as a select agent.

After a 1995 incident in which an individual in the United States unlawfully obtained *Yersinia pestis*, the bacterium that causes plague, Congress enacted section 511 of the Antiterrorism and Effective Death Penalty Act of 1996.² This statute directed the HHS Secretary to promulgate regulations identifying a list of biological agents that have the potential to pose a severe threat to public health and safety, providing procedures governing the transfer of those agents, and establishing safeguards to prevent unauthorized access to those agents for

¹ *Evaluation of DoD Biological Safety and Security Implementation* (DODIG-2016-078), Apr. 7, 2016. See <https://media.defense.gov/2016/Apr/27/2001714233/-1/-1/1/DODIG-2016-078.pdf> (accessed Sep. 20, 2018).

² P.L. No. 104-132 (enacted Apr. 24, 1996).

purposes of terrorism or other criminal activities. The HHS Secretary delegated the authority to regulate select agents to the Centers for Disease Control and Prevention (CDC), which then delegated its authority under this statute to its Division of Select Agents and Toxins (DSAT) and established the CDC Select Agent Program.

After the September 11, 2001, terrorist events and the anthrax attacks, Congress passed the Public Health Security and Bioterrorism Preparedness and Response Act of 2002.³ This statute expanded HHS's authority to regulate the transfer, use, and possession of select agents and granted similar authority to USDA for select agents that pose a threat to animal or plant health or to animal or plant products. USDA delegated its authority to the Animal and Plant Health Inspection Service (APHIS), which established the Agriculture Select Agent Services (AgSAS).

The Federal Select Agent Program

Together, DSAT and AgSAS jointly manage the Federal Select Agent Program (FSAP). FSAP regulates the possession, use, and transfer of biological agents listed in 7 CFR part 331, 9 CFR part 121, and 42 CFR part 73.⁴ FSAP enhances the Nation's oversight of the safety and security of select agents by:

- developing, implementing, and enforcing select agent regulations;
- maintaining a national database of registered entities that possess select agents;
- inspecting entities that possess, use, or transfer select agents;
- ensuring that all individuals who work with these agents undergo a security risk assessment performed by the Federal Bureau of Investigation (FBI) Criminal Justice Information Service;
- providing guidance to regulated entities by developing guidance documents and conducting workshops and webinars; and
- investigating incidents in which noncompliance may have occurred.

Registered Entities

Any laboratory working with select agents must register with FSAP to become a registered entity. All laboratories must comply with Federal regulations regarding biosafety and security if they anticipate working with select agents.

To register to possess select agents, an entity must submit an application package to FSAP, and entity personnel must submit to a security risk assessment conducted by the FBI. FSAP conducts an on-site inspection before issuing a new certificate of registration or renewing an

³ P.L. No. 107-188 (enacted June 12, 2002).

⁴ See Appendix C for a summary of Federal requirements referenced in this report.

existing registration. Once approved, an entity's registration is valid for a maximum of 3 years and may be amended to reflect changes in circumstances such as the replacement of the Responsible Official; changes in ownership, control, or select agent activities; or the addition or removal of any select agents.

As a condition of registration, select agent regulations require registered entities to designate an individual as the Responsible Official who ensures compliance with regulations. In addition, the select agent regulations require entities to develop written plans, provide training, and maintain records of training and other activities. As part of the requirement that registered entities develop written plans, registered entities must develop and implement a written security plan that is sufficient to safeguard each select agent against unauthorized access, theft, loss, or release and develop and implement a written biological safety plan that is commensurate with the risk of the registered entity's select agents given their intended use. Additionally, registered entities are required to provide training on biological safety and security for individuals with access to select agents and maintain records on the training provided to each individual with access to select agents and other activities covered by the select agent regulations.

To transfer a select agent, the registered entities involved in the transfer must obtain an authorization from FSAP. To obtain the authorization, FSAP requires both the shipping and receiving entities to complete the APHIS/CDC Form 2, Request To Transfer Select Agents and Toxins.⁵ Before any transfer can occur, both the shipping and receiving entities must fill out applicable sections of the Form 2 and send it to FSAP for authorization. When the shipment is complete, the receiving entity fills out another section of the form and sends a copy of the completed Form 2 to both the shipping entity and FSAP. FSAP guidance on completing the Form 2 includes some of the requirements for select agent transfers; these requirements are also listed in the Federal select agent regulations.

The Food and Drug Administration

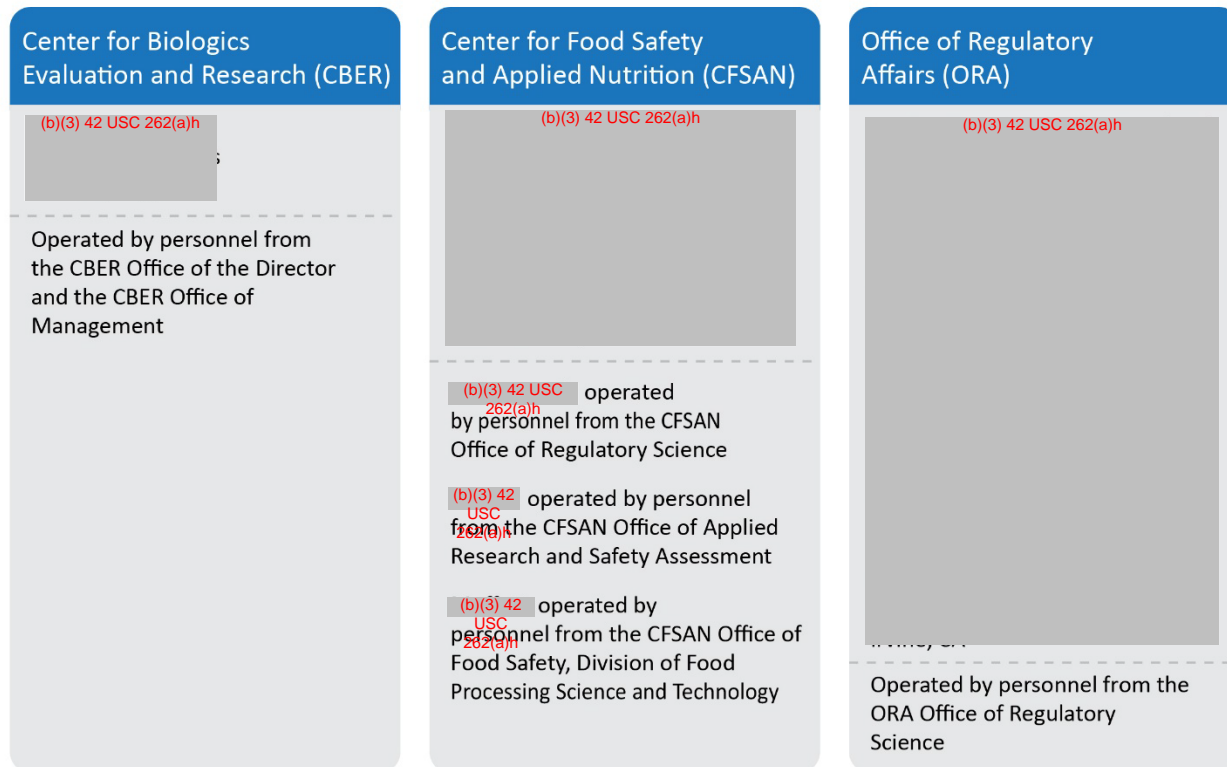
FDA is responsible for the oversight of medical products, food, cosmetics, tobacco, dietary supplements, and products that give off radiation. In 2015, FDA had approximately 16,000 employees and a budget of \$4.5 billion. FDA has campuses throughout the United States. All FDA laboratories that work with select agents and are located on the same campus are registered as one select agent registered entity.

During the audit period, FDA had 11 total registered entities within the Center for Biologics Evaluation and Research (CBER), the Center for Food Safety and Applied Nutrition (CFSAN), and

⁵ In addition to requesting authorization, this form provides the shipping and receiving entities and FSAP with documentation of important aspects of the transfer. This documentation includes a list of each select agent being transferred, the names of shipping entity personnel involved in the shipping process, the address of the shipping entity, the date the select agent or agents were shipped, a description of the packaging, the name of the carrier, the name of the individual who received the shipment, and a statement from that individual about what was received, whether the packaging was damaged, whether the select agent or agents were packaged in accordance with all laws and regulations, and the date the package was received.

the Office of Regulatory Affairs (ORA). FDA does not fund select agent work at organizations outside of FDA. Figure 1 below shows how FDA’s 11 registered entities were organized during the audit period.

Figure 1: FDA’s Registered Entities



After the start of our review, (b)(3) 42 USC 262(a)h, and (b)(3) 42 USC 262(a)h terminated their select agent registrations on July 11, 2016, October 25, 2016, and December 7, 2016, respectively. (b)(3) 42 USC 262(a)h never had any select agents and only registered with FSAP in case it needed to function as a registered entity at a later date.

In February 2017, FDA established the Office of Laboratory Science and Safety (OLSS) within the Office of the Commissioner as the single point of accountability for all laboratory science, laboratory security, environmental, occupational safety, and health programs. FDA officials stated that OLSS will provide agency-wide oversight to ensure that all of FDA’s registered entities comply with all FSAP-associated statutes and regulations.

HOW WE CONDUCTED THIS REVIEW

We examined select agent shipment policies and protocols in place at FDA’s registered entities by reviewing eight select agent shipments either shipped or received by FDA’s registered entities during the 2-year period from October 1, 2013, through September 30, 2015. We also requested documentation of all inactivated select agents shipped and received during the same period. We reviewed FDA policies, training documentation, and select agent transfer

transactions and inactivations⁶ for compliance with requirements at 42 CFR part 73 and FSAP guidance. We also evaluated these FDA select agent transfers by reviewing information on all Form 2 documents.

We conducted this performance audit in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

See Appendix A for the details of our audit scope and methodology and Appendix D for information related to select agent shipments we reviewed as part of our audit.

FINDINGS

Generally, FDA has designed and put in place controls to ensure that select agent shipments are prepared and received in accordance with Federal regulations and related supporting laboratory guidance and instruction. However, we found that not all of FDA's registered entities' security plans included certain FSAP notification procedures. Specifically, we found that most of FDA's registered entities' security plans did not include procedures for notifying FSAP if a select agent shipment is not received within 48 hours after the expected delivery time, if a select agent shipment receives damage to the extent that a select agent release may have occurred, or if an authorization for a select agent transfer expires or becomes void before the shipment is completed. We also found that two of FDA's registered entities did not verify or maintain all documentation showing that their personnel understood required select agent training on biosafety, security, and incident response. Finally, we found that FDA's registered entities did not have sufficient policies to ensure compliance with all new inactive select agent shipment requirements.

REGISTERED ENTITIES' SECURITY PLANS DID NOT INCLUDE CERTAIN PROCEDURES

Eight Registered Entities' Security Plans Did Not Include Procedures for Notifying the Federal Select Agent Program if a Select Agent Shipment Is Not Received Within 48 Hours of the Expected Delivery Time

Federal regulations require that a registered entity should immediately notify FSAP if a select agent shipment is not received within 48 hours after the expected delivery time (42 CFR § 73.16(j)). Additionally, Federal regulations provide that a registered entity must have its own written security plan containing procedures for reporting unauthorized or suspicious persons or activities, loss or theft of select agents or toxins, or release of select agents or toxins (42 CFR § 73.11(c)(6)). The security plans must also contain provisions and policies for shipping,

⁶ An inactivation is defined as a procedure to render a select agent or a regulated nucleic acid nonviable or non-toxic while retaining one or more characteristics of interest for future use.

receiving, and storing select agents and toxins (42 CFR § 73.11(c)(10)). Security plans must also be tested and evaluated annually (42 CFR § 73.11(h)).

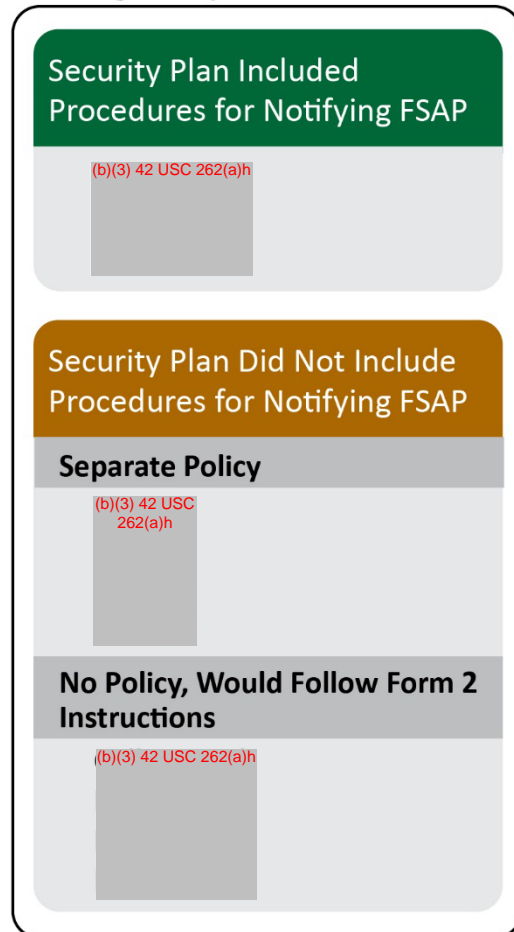
We found that most of FDA’s registered entities’ security plan procedures for preparing and receiving select agent shipments did not include procedures for notifying FSAP if a select agent shipment is not received within 48 hours after the expected delivery time.⁷ Although the (b)(3) 42 USC 262(a)h and (b)(3) 42 USC 262(a)h included notification procedures in their security plans, (b)(3) 42 USC 262(a)h did not.

(b)(3) 42 USC 262(a)h had policies separate from their security plans that included procedures for notifying FSAP if the registered entity does not receive a select agent shipment within 48 hours of the time it is expected. However, having a separate policy does not negate the need to include these procedures in registered entities’ security plans. It is not sufficient for registered entities to include these procedures only in policies separate from their security plan because regulations do not always require that separate policies be maintained.

Officials at (b)(3) 42 USC 262(a)h stated that these registered entities do not need to include these procedures in their security plans because personnel would follow guidance outlined in the Form 2 instructions. Those instructions state that if a select agent shipment is not received within 48 hours of the time it was expected to be received, the receiving entity must contact FSAP and submit to FSAP a completed APHIS/CDC Form 3, Report of Theft, Loss, or Release of Select Agents and Toxins. While the Form 2 instructions address the 48-hour reporting procedures, the instructions are not a substitute for including procedures in registered entities’ security plans. The instructions for the Form 2 are insufficient because they are separate from the actual form, and there is no way to know how frequently recipients actually review the instructions.

Security plans are required, site-specific, and must be annually tested and evaluated to ensure their effectiveness in safeguarding select agents. Therefore, security plans that describe how, when, and why intended recipients need to notify the Responsible Official should further ensure that FSAP receives timely notification of any theft, loss, or release. Timely reporting to

Figure 2: Not All Security Plans Had FSAP Notification Procedures for Untimely Select Agent Shipment Deliveries



⁷ See Figure 2 for explanations that FDA’s registered entities provided for how they addressed the need for these security plan procedures.

FSAP should help safeguard select agents and ensure that FSAP initiates an investigation to locate the package. A lack of 48-hour reporting procedures in registered entities' security plans could result in a missing or stolen select agent package either not being reported to FSAP or not being reported to FSAP within 48 hours, which could delay the start of an important investigation to locate the package.

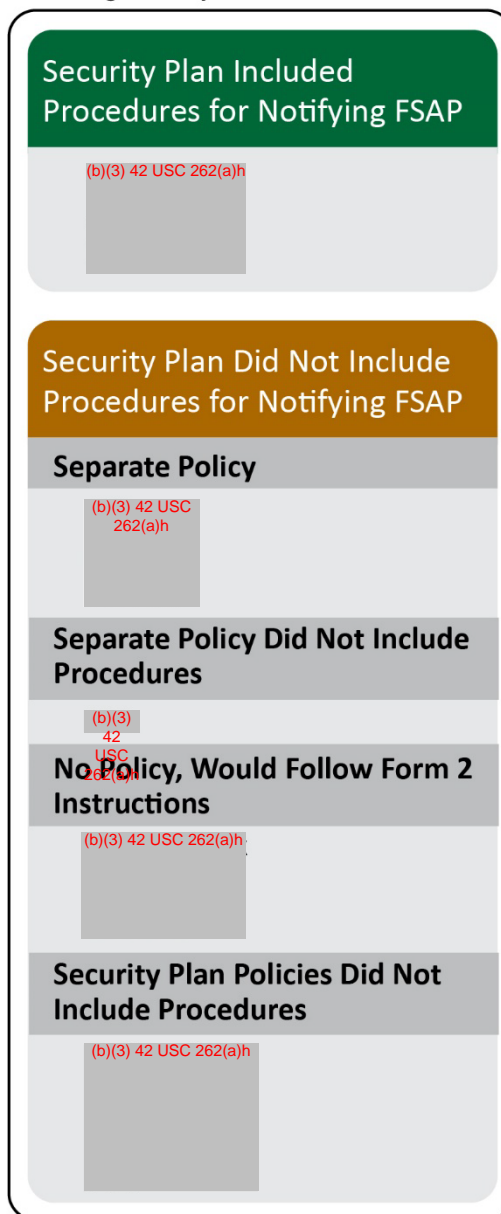
Eight Registered Entities' Security Plans Did Not Include Procedures for Notifying the Federal Select Agent Program if a Damaged Select Agent Shipment Is Received

Federal regulations require that a registered entity immediately notify FSAP if a select agent shipment is received that is damaged to the extent that the release of a select agent may have occurred (42 CFR § 73.16(j)). Additionally, Federal regulations state that a registered entity must have its own written security plan containing procedures for reporting unauthorized or suspicious persons or activities, loss or theft of select agents or toxins, and release of select agents or toxins (42 CFR § 73.11(c)(6)). The security plan must also contain provisions and policies for shipping, receiving, and storing select agents and toxins (42 CFR § 73.11(c)(10)). Security plans must also be tested and evaluated annually (42 CFR § 73.11(h)).

We found that most of FDA's registered entities' security plan procedures for preparing and receiving select agent shipments did not include procedures for notifying FSAP if a select agent shipment is received that is damaged to the extent that the release of a select agent may have occurred.⁸ Although the [redacted] included notification procedures in their security plans, [redacted] did not.

[redacted] had policies separate from their security plans that included procedures for notifying FSAP if the registered entity received a damaged select agent shipment, and [redacted] had a damaged package policy in its separate biosafety plan. However, we found that [redacted] policy did not

Figure 3: Not All Security Plans Had FSAP Notification Procedures for Damaged Select Agent Shipments



⁸ See Figure 3 for explanations that FDA's registered entities provided for how they addressed the need for these security plan procedures.

require reporting damaged select agent shipments to FSAP. As previously stated, having a separate policy does not negate the need to include these procedures in registered entities' security plans.

Officials at (b)(3) 42 USC 262(a)h stated that these registered entities do not need to include these procedures in their security plans because personnel would follow guidance outlined in the Form 2 instructions. Those instructions state that if a registered entity receives a select agent shipment that is damaged to the extent that a select agent release may have occurred, it must contact FSAP immediately and submit to FSAP a completed Form 3. While the Form 2 instructions address receiving damaged shipments, the instructions are not a substitute for including procedures in registered entities' security plans. As previously stated, the instructions for the Form 2 are insufficient because they are separate from the actual form, and there is no way to know how frequently recipients actually review the instructions.

In addition, officials at (b)(3) 42 USC 262(a)h stated that these registered entities have policies related to damaged shipments in their security plans; however, we found that those policies do not require notifying FSAP. Officials at (b)(3) 42 USC 262(a)h stated that it has a policy in its security plan, but we found that the policy is related to theft, loss, and release and does not specifically mention damaged select agent shipments. Having security plan procedures for theft, loss, and release does not negate the need to have a specific policy on damaged select agent shipments.

A lack of security plan procedures requiring registered entities to notify FSAP about damaged select agent shipments increases the potential that registered entities might not report a damaged shipment to FSAP, and a lack of reporting could cause a delay in containing a select agent release.

All Registered Entities' Security Plans Did Not Include Procedures for Notifying the Federal Select Agent Program if an Authorization for a Select Agent Transfer Expires

Federal regulations state that approval of the transfer of a select agent is valid for 30 days from the date of authorization (42 CFR § 73.16(k)). This means that the transfer of the select agent must be completed before expiration of the 30-day period. Approval of a transfer becomes void should there be a change in any of the conditions upon which the approval was based (e.g., a change in the certificate of registration for the shipping entity or receiving entity or a change in the application for transfer) (42 CFR § 73.16(k)). FSAP provides each transfer an authorization number that is valid for only one transfer of select agents or toxins during the 30-day period. Federal regulations state that transportation ends when the package is received by an intended recipient approved to have access to select agents and toxins (42 CFR § 73.16(h)). However, CDC officials stated that in practice, shipments that extend beyond 30 days are allowed to be completed if the shipment is initiated before the end of the 30-day period.

Additionally, Federal regulations provide that a registered entity must have its own written security plan containing procedures for reporting unauthorized or suspicious persons or

activities, loss or theft of select agents or toxins, and release of select agents or toxins (42 CFR § 73.11(c)(6)), as well as provisions and policies for shipping, receiving, and storing select agents and toxins (42 CFR § 73.11(c)(10)).

We found that none of FDA’s registered entities’ security plan procedures for preparing and receiving select agent shipments included procedures for notifying FSAP if a select agent transfer is not completed within 30 calendar days after issuance or if the facts supporting the authorization change before the select agent transfer is completed.⁹

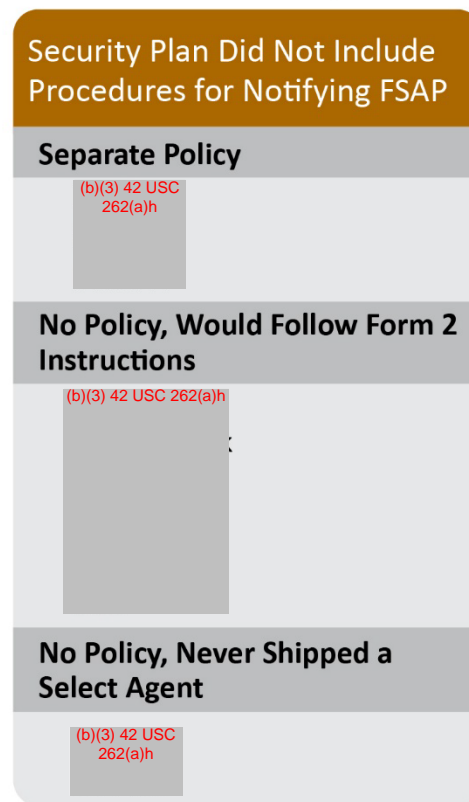
(b)(3) 42 USC 262(a)h each had policies separate from their security plans that included procedures for notifying FSAP if a select agent shipment is not completed within the 30-day authorization period. As previously stated, having a separate policy does not negate the need to include these procedures in registered entities’ security plans.

Officials at the (b)(3) 42 USC 262(a)h stated that these registered entities do not need to include these procedures in their security plans because personnel would follow guidance outlined in the Form 2 instructions. The instructions state that a registered entity has 30 calendar days to complete an approved transfer and further state that if the transfer does not occur, the receiving entity’s Responsible Official must complete Block 42 of the Form 2 and return to FSAP the signed and dated Form 2. While the Form 2 instructions address reporting a transfer that is not completed before an authorization expires or becomes void, the instructions are not a substitute for including procedures in registered entities’ security plans. As previously stated, the instructions for the Form 2 are insufficient because they are separate from the actual form, and there is no way to know how frequently recipients actually review the instructions.

Officials at (b)(3) 42 USC 262(a)h stated that these registered entities have never shipped a select agent. Regardless of whether they have ever shipped select agents, all registered entities need to include these procedures in their security plans because they may ship a select agent in the future.

A lack of security plan procedures for reporting a transfer that is not completed before an authorization expires or becomes void could result in a registered entity not returning the

Figure 4: Security Plans Did Not Have FSAP Notification Procedures for Expired Authorizations for Select Agent Transfers



⁹ See Figure 4 for explanations that FDA’s registered entities provided for how they addressed the need for these security plan procedures.

Form 2 notifying FSAP that the transfer never occurred. If an authorization remains open, there is a potential that a registered entity could receive a shipment of a select agent it has neither recently requested nor coordinated and therefore is not expecting.

SOME REGISTERED ENTITIES DID NOT MAINTAIN REQUIRED SELECT AGENT TRAINING DOCUMENTATION SHOWING THAT PERSONNEL UNDERSTOOD ALL TRAINING

Federal regulations require that a registered entity must provide information and training on biosafety, security and security awareness, and incident response to each individual with approval to access select agents and toxins before that individual is given access to them (42 CFR § 73.15). The training must address the particular needs of the individual, the work he or she will do, and the risks posed by the select agents or toxins (42 CFR § 73.15(a)(1)). Additionally, regulations require that annual refresher training be provided for individuals with access approval; these personnel must also receive refresher training if the registered entity significantly amends its security, incident response, or biosafety plans (42 CFR § 73.15(c)). The Responsible Official ensures that the entity maintains a record of the training provided to each individual with access to select agents and toxins and to each escorted individual (e.g., a laboratory worker or visitor) (42 CFR § 73.15(d)). The record must include the name of the individual trained, the date of the training, a description of the training provided, and the means used to verify that the individual understood the training (42 CFR § 73.15(d)). An individual's access may be revoked if it is determined that such action is necessary to protect public health and safety (42 CFR § 73.10(h)(2)).

Although most of FDA's registered entities documented that personnel had properly completed their required training and understood it, (b)(3) 42 USC 262(a)h did not verify or maintain all documentation that personnel understood the required training. When we requested documentation, (b)(3) 42 USC 262(a)h supplied some ungraded tests for the required training. After we discussed the ungraded tests with FDA personnel, (b)(3) 42 USC 262(a)h supplied the same tests we received before; however, the tests had been graded. Although the newly graded tests documented that personnel understood the required training, (b)(3) 42 USC 262(a)h had not verified and maintained this documentation during the audit period.

Without verification and maintenance of the required training documentation, registered entities cannot assess and ensure that their personnel understood the required select agent training. Personnel who do not understand the training may take incorrect action regarding select agents and may pose a risk to public health and safety.

REGISTERED ENTITIES DID NOT HAVE SUFFICIENT POLICIES TO ENSURE COMPLIANCE WITH ALL NEW INACTIVE SELECT AGENT SHIPMENT REQUIREMENTS

During the audit period, FDA's registered entities did not record inactivation of select agents because there were no regulations requiring the laboratories to do so. However, Federal regulations at 42 CFR section 73.17(a)(8), effective March 21, 2017, require additional recordkeeping for nonviable and shipped select agents. The new regulation requires a certificate signed by the principal investigator detailing who inactivated the select agent and

how it was inactivated. The certificate must travel with the inactivated select agent when it is transferred. In addition to the certificate, an entity must record a description of the inactivation procedure, a description of the viability testing protocol used to determine that an inactivated select agent no longer contains viable select agent material, the names of the personnel who inactivated the select agent, and the date and location of the inactivation.

OLSS issued a directive on October 5, 2017, requiring FDA's registered entities to follow all FSAP requirements. The directive included a sample of the certificate for FDA's registered entities to use. The sample FDA certificate specifies that the certificate must describe the inactivation procedure, provide the date that the inactivation procedure occurred, state that the inactivation was confirmed by an approved viability testing protocol, and be signed by the principle investigator. However, the directive does not specify that registered entities must also record a description of the viability testing, the names of the personnel who inactivated the select agent, and the location of the inactivation. FDA officials stated that none of FDA's registered entities had ever shipped an inactivated select agent. However, if FDA's registered entities do inactivate and ship select agents, they could overlook required recording procedures because the directive does not specify those FSAP requirements.

RECOMMENDATIONS

We recommend that FDA:

- update its registered entities' security plans to include procedures for notifying FSAP if a select agent:
 - shipment is not received within 48 hours after the expected time of delivery,
 - package is received damaged to the extent that a release of the select agent may have occurred,
 - shipment will not be completed within 30 calendar days after transfer authorization issuance, or
 - transfer authorization becomes void because the facts supporting the authorization changed;
- ensure that its registered entities verify and maintain documentation to assure that employees who are required to have select agent training understand the training received; and
- update its policies for shipping inactivated select agents to require that its registered entities record a description of the viability testing protocol used, the names of the personnel who inactivated the select agent, and the location of the inactivation.

FDA COMMENTS

In written comments on our draft report, FDA concurred with our recommendations and stated that it has taken actions to implement them. FDA said that it has developed a standardized template for the Select Agent Security Plan used by ORA and the FDA Centers that participate in FSAP that addresses all of our recommendations. FDA also stated that OLSS Directive 201710.2 was amended to address all of the recommendations. Finally, FDA provided technical comments on our draft report that we have addressed in this report as appropriate.

FDA's comments, excluding the technical comments, are included as Appendix E.

APPENDIX A: AUDIT SCOPE AND METHODOLOGY

SCOPE

Our review covered select agent transfer and inactivated select agent transfer transactions that took place at FDA from October 1, 2013, through September 30, 2015. We compared FDA's registered entities' shipping and receiving policies to the select agent requirements at 42 CFR part 73 and related FSAP guidance.

We conducted our fieldwork from May 2016 through October 2018.

METHODOLOGY

To accomplish our objective, we:

- reviewed applicable Federal laws, regulations, and guidance;
- discussed the FDA select agent program background with FDA personnel;
- reviewed all FDA policies related to shipping and receiving select agents, select agent training, and select agent inactivations and compared them to Federal regulations;
- reviewed all select agent shipping and receiving transactions and associated documentation and communications;
- requested a list of all inactivated, shipped, and received select agents;
- reviewed validations of methods for inactivating select agents;
- reviewed select agent training policies, content, and attestations stating that personnel understood the required trainings;
- reviewed select agent training documentation, certifications, and test scores for a judgmental sample of FDA personnel involved in select agent shipping, receiving, and inactivation;
- communicated with FSAP personnel about FSAP requirements; and
- discussed the results of our review with FDA officials.

We conducted this performance audit in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

APPENDIX B: RELATED OFFICE OF INSPECTOR GENERAL REPORTS

Report Title	Report Number	Date Issued
<i>The National Institutes of Health Generally Complied With Federal Requirements for the Preparation and Receipt of Select Agent Shipments</i>	<u>A-03-15-00354</u>	12/4/2018
<i>Summary Report on State, Local, Private, and Commercial Laboratories' Compliance With Select Agent Regulations</i>	<u>A-04-06-01033</u>	1/9/2008
<i>Summary Report on Universities' Compliance With Select Agent Regulations</i>	<u>A-04-05-02006</u>	6/30/2006
<i>Summary Report on Select Agent Security At Universities</i>	<u>A-04-04-02000</u>	3/25/2004

APPENDIX C: FEDERAL REQUIREMENTS

42 CFR §§ 73.10(h) and 73.10(h)(2), Restricting access to select agents and toxins; security risk assessments

“(h) An individual's access approval may be denied, limited, or revoked if: . . . (2) It is determined such action is necessary to protect public health and safety.”

42 CFR § 73.11, Requirements for security plans

(a) An individual or entity required to register under this part must develop and implement a written security plan. The security plan must be sufficient to safeguard the select agent or toxin against unauthorized access, theft, loss, or release. . . .

(c) The security plan must . . . (10) 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 provisions must provide that an entity will properly secure containers on site and have a written contingency plan for unexpected shipments . . .

(d) . . . (5) Establish a protocol for intra-entity transfers under the supervision of an individual with access approval from the HHS Secretary or Administrator, including chain-of-custody documents and provisions for safeguarding against theft, loss, or release . . .

(f) In addition to the requirements contained in paragraphs (c) and (d) of this section, the security plan for an individual or entity possessing a Tier 1 select agent or toxin^[10] must also: (1) Describe procedures for conducting a pre-access suitability assessment of persons who will have access to a Tier 1 select agent or toxin. . . .

(h) The plan must be reviewed annually and revised as necessary. Drills or exercises must be conducted at least annually to test and evaluate the effectiveness of the plan. The plan must be reviewed and revised, as necessary, after any drill or exercise and after any incident.

¹⁰ Tier 1 select agents are biological agents and toxins that represent the greatest risk of deliberate misuse; have significant potential for mass casualties or devastating effects to the economy, critical infrastructure, or the public confidence; and pose a severe threat to public health and safety. Entities that possess, use, or transfer Tier 1 select agents must adhere to the additional requirements detailed within the Federal select agent regulations.

42 CFR § 73.15, Training requirements for people with access to select agents

(a) An individual or entity required to register under this part must provide information and training on biocontainment, biosafety, security (including security awareness), and incident response to:

(1) Each individual with access approval from the HHS Secretary or Administrator. 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. The training must be accomplished prior to the individual's entry into an area where a select agent is handled or stored, or within 12 months of the date the individual was approved by the HHS Secretary or the Administrator for access, whichever is earlier.

(2) Each individual not approved for access to select agents and toxins by the HHS Secretary or Administrator before that individual enters areas under escort 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. The training must be accomplished prior to the individual's entry into 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.).

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

(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.

(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.

42 CFR § 73.16(j), Transfers

“The recipient must immediately notify CDC or APHIS if the select agent or toxin has not been received within 48 hours after the expected delivery time, or if the package containing select

agents or toxins has been damaged to the extent that a release of the select agent or toxin may have occurred.”

42 CFR § 73.16(k), Transfers

“An authorization for a transfer shall be valid only for 30 calendar days after issuance, except that such an authorization becomes immediately null and void if any facts supporting the authorization change (e.g., change in the certificate of registration for the sender or recipient, change in the application for transfer).”

42 CFR § 73.17, Records

(a) An individual or entity required to register under this part must maintain complete records relating to the activities covered by this part. Such records must include: . . . (8) For select agents or material containing select agents or regulated nucleic acids that can produce infectious forms of any select agent virus that have been subjected to a validated inactivation procedure or a procedure for removal of viable select agent: (i) A written description of the validated inactivation procedure or viable select agent removal method used, including validation data; (ii) A written description of the viability testing protocol used; (iii) A written description of the investigation conducted by the entity Responsible Official involving an inactivation or viable select agent removal failure and the corrective actions taken; (iv) The name of each individual performing the validated inactivation or viable select agent removal method; (v) The date(s) the validated inactivation or viable select agent removal method was completed; (vi) The location where the validated inactivation or viable select agent removal method was performed; and (vii) A certificate, signed by the Principal Investigator, that includes the date of inactivation or viable select agent removal, the validated inactivation or viable select agent removal method used, and the name of the Principal Investigator. A copy of the certificate must accompany any transfer of inactivated or select agent removed material.

APPENDIX D: FDA SELECT AGENT TRANSFERS

	Entity	Shipping Entity (S)/ Receiving Entity (R)	Packaged Correctly	Form 2 Properly Signed	Shipment Received Within Expected Time	Transfer Completed Within 30 Days	Employee Training Documents Provided
1	CFSAN (b)(3) 42 USC 262(a)h	R	Y	Y	Y	Y	Y
2	CFSAN (b)(3) 42 USC 262(a)h	S	Y	Y	Y	Y	Y
3	CFSAN (b)(3) 42 USC 262(a)h	S	Y	Y	Y	Y	Y
4	CFSAN (b)(3) 42 USC 262(a)h	R	Y	Y	Y	Y	Y
5	CFSAN (b)(3) 42 USC 262(a)h	R	Y	Y	Y	Y	Y
6	CFSAN (b)(3) 42 USC 262(a)h	R	Y	Y	Y	Y	Y
7	CFSAN (b)(3) 42 USC 262(a)h	S	Y	Y	Y	Y	Y
8	CFSAN (b)(3) 42 USC 262(a)h	S	Y	Y	Y	Y	Y

APPENDIX E: FDA COMMENTS



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

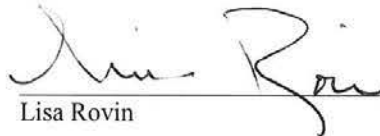
DATE: April 29, 2019

TO: Daniel R. Levinson
Inspector General

FROM: Lisa Rovin, JD
Director, Office of Public Health Strategy and Analysis

SUBJECT: Food and Drug Administration's Response to Office of Inspector General Draft Report: The Food and Drug Administration Generally Complied with Federal Requirements for the Preparation and Receipt of Select Agent Shipments, Report A-03-16-00354

The Food and Drug Administration (FDA) appreciates the opportunity to review and comment on the Office of Inspector General's (OIG) draft report entitled, "The Food and Drug Administration Generally Complied with Federal Requirements for the Preparation and Receipt of Select Agent Shipments."



Lisa Rovin

Attachment

Food and Drug Administration General Comments to

Office of Inspector General Draft Report

“The Food and Drug Administration Generally Complied with Federal Requirements for the Preparation and Receipt of Select Agent Shipments, Report A-03-16-00354)

The Food and Drug Administration (FDA) welcomes the Office of the Inspector General’s (OIG) report as a means for assessing FDA’s controls for ensuring that select agents are prepared and received in accordance with the Federal Select Agent Program (FSAP). The Office of Laboratory Science and Safety (OLSS) is committed to ensuring that all FDA Select Agent facilities fully comply with the FSAP. OLSS reviewed OIG’s findings and recommendations and has already taken steps to implement these recommendations. We will update OIG as they are completed.

OIG Recommendation 1: *Update its registered entities’ security plans to include procedures for notifying the Federal Select Agent Program (FSAP) if the select agent shipment is not received within 48 hours after the expected time of delivery.*

FDA Response: FDA concurs with this recommendation. OLSS has developed a standardized template for the Select Agent Security Plan being used throughout all FDA Centers and the Office of Regulatory Affairs (ORA) participating in the Federal Select Agent Program. The new template states “if the BSATs are not received within 48 hours after the expected delivery time or if the package(s) received containing BSATs has/have been damaged to the extent that a release of the BSAT(s) may have occurred, the recipient’s RO must immediately report this to APHIS/CDC and submit a completed APHIS/CDC Form 3 to APHIS/CDC via eFSAP.” This language has been updated in the Center for Biologics Evaluation and Research (CBER) and ORA plans which are undergoing finalization, and the Center for Food Safety and Applied Nutrition (CFSAN) plans are currently being updated and will be completed within the next two months.

Recommendation 2: *Update its registered entities’ security plans to include procedures for notifying the Federal Select Agent Program (FSAP) if the select agent package is received damaged to the extent that a release of the select agent may have occurred.*

FDA Response: FDA concurs with this recommendation. OLSS has developed a standardized template for the Select Agent Security Plan being used throughout all FDA Centers and the Office of Regulatory Affairs (ORA) participating in the Federal Select Agent Program. The new template states “f the BSATs are not received within 48 hours after the expected delivery time or if the package(s) received containing BSATs has/have been damaged to the extent that a release of the BSAT(s) may have occurred, the recipient’s RO must immediately report this to APHIS/CDC and submit a completed APHIS/CDC Form 3 to APHIS/CDC via eFSAP.” This language has been updated in CBER and ORA plans which are undergoing finalization, and CFSAN plans are currently being updated and will be completed within the next two months.

Recommendation 3: *Update its registered entities' security plans to include procedures for notifying the Federal Select Agent Program (FSAP) if a select agent shipment transfer authorization becomes void because the facts supporting the authorization have changed.*

FDA Response: FDA concurs with this recommendation. OLSS has developed a standardized template for the Select Agent Security Plan to be used throughout all FDA Centers and the Office of Regulatory Affairs (ORA) participating in the Federal Select Agent Program. The new template states, "Transfer authorizations become void if the facts supporting the authorization change and FSAP will be notified." This language has been updated in CBER and ORA plans which are undergoing finalization, and CFSAN plans are currently being updated and will be completed within the next two months.

Recommendation 4: *Update its registered entities' security plans to include procedures for notifying the Federal Select Agent Program (FSAP) if a select agent shipment will not be completed within 30 calendar days after transfer authorization issuance.*

FDA Response: FDA concurs with this recommendation. OLSS has developed a standardized template for the Select Agent Security Plan being used throughout all FDA Centers and the Office of Regulatory Affairs (ORA) participating in the Federal Select Agent Program. The new template states, "Approval for an entity to transfer a BSAT is valid for only one transfer. The actual transfer must be completed within 30 days from the date of FSAP authorization. A notification to FSAP is required if a select agent shipment is not completed within the 30-days authorization period. Multiple transfers of a BSAT occurring on different days require separate FSAP authorizations for each transfer." This language has been updated in CBER and ORA plans which are undergoing finalization, and CFSAN plans are currently being updated and will be completed within the next two months.

Recommendation 5: *Ensure that its registered entities verify and maintain documentation to assure that employees who are required to have select agent training understand the training received.*

FDA Response: FDA concurs with this recommendation. OLSS has developed a standardized template for the Select Agent Security Plan to be used throughout all FDA Centers and the Office of Regulatory Affairs (ORA) participating in the Federal Select Agent Program. The new template states, "Records of training for each individual must be kept for three years in compliance with the Select Agent Regulations. 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." This language has been updated in CBER and ORA plans which are undergoing finalization and CFSAN plans are currently being updated and will be completed within the next two months.

Recommendation 6: *Update its policies for shipping inactivated select agents to require that its registered entities record a description of the viability testing protocol used, the names of the personnel who inactivated the select agent, and the location of the inactivation.*

FDA Response: FDA concurs with this recommendation. OLSS Directive 201710.2 (attached) was amended to address all of OIG's recommendations. Additionally, language has also been incorporated into the OLSS-developed standardized template for the Select Agent Security Plan to be used throughout all FDA Centers and ORA participating in the Federal Select Agent Program.