



2016

# Annual Report of the Federal Select Agent Program



U.S. Department of Health and Human Services  
Centers for Disease Control and Prevention

U.S. Department of Agriculture  
Animal and Plant Health Inspection Service

## Table of Contents

Executive Summary .....	3
Acronyms .....	8
Introduction .....	9
Key Program Statistics .....	9
Registration .....	9
Registered Entities .....	9
New Registrations .....	11
Renewals .....	12
Entity Withdrawals .....	12
Tier 1 BSAT .....	12
<i>Bacillus anthracis</i> .....	12
Entities registered for <i>Bacillus cereus</i> Biovar anthracis .....	12
Waivers for inactivated <i>Bacillus anthracis</i> and <i>Bacillus cereus</i> Biovar anthracis material .....	13
Top 10 Agents Registered With Each Agency .....	13
Laboratory Types .....	14
Security Risk Assessments .....	14
Inspection Data .....	16
Inspections .....	16
Length of Inspections .....	16
Inspection Findings and Compliance .....	17
Corrective Action Plan .....	17
Registration Suspensions .....	18
Reports and Referrals .....	19
Confidential Reporting System .....	19
Referrals to HHS OIG or APHIS IES .....	19
FBI Notifications .....	19
Restricted Experiments .....	20
Exclusions .....	21
Report of the Identification of a Select Agent or Toxin .....	22
Transfers of Select Agents or Toxins .....	23
Theft, Loss, and Release of Select Agents and Toxins .....	27
Emergency Response .....	28
Federal Register Notices, Policy Statements, and Guidance .....	29
Outreach .....	29
References .....	30

## Executive Summary

The Federal Select Agent Program (FSAP) is managed jointly by the Department of Health and Human Services (HHS), Centers for Disease Control and Prevention (CDC), Division of Select Agents and Toxins (DSAT); and the United States Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS), Agriculture Select Agent Services (AgSAS). FSAP oversees the possession, use, and transfer of biological select agents and toxins (BSAT) so that research with these materials can be conducted as safely and securely as possible. This research provides important scientific discoveries to develop countermeasures and improve detection, prevention, diagnostic, and treatment options for diseases caused by these BSAT, which are considered to be some of the most threatening to public and agricultural health. DSAT oversees the regulation of BSAT that pose a severe threat to human health while AgSAS oversees the regulation of BSAT that pose a severe threat to animal and plant health, as well as animal and plant products.

In October 2015, the United States Government released two sets of complementary recommendations to improve the oversight of the safety and security at laboratories that work with BSAT, one from the [Federal Experts Security Advisory Panel](#) (FESAP) and another from the [Fast Track Action Committee on Select Agent Regulations](#) (FTAC-SAR). CDC also released its own recommendations for program improvement through a [90-day Internal Review of the Division of Select Agents and Toxins](#). All three reviews provided recommendations, including that FSAP increase transparency and public engagement and improve communication with the regulated community. Since those reviews were released, FSAP has implemented many of the recommendations and has periodically provided progress updates [online](#). This report summarizes calendar year 2016 FSAP data and is FSAP's second report of aggregate data, reflecting the program's ongoing commitment to increasing transparency and understanding of the program.

### Registered Entities

As of December 31, 2016, 276 entities were registered with FSAP: 38 entities registered with AgSAS as the lead agency and 238 entities registered with DSAT as the lead agency.

An entity may choose to register with either AgSAS or DSAT as the lead agency based on the BSAT that they are registered to possess. During 2016, the registration of 51 of the 276 entities were jointly managed by AgSAS and DSAT with AgSAS serving as the lead agency for 14 of those entities and DSAT serving as the lead agency for 37 of those entities.

Regulated entities during calendar year 2016 consisted of:

- 32% academic
- 29% non-federal government
- 18% commercial
- 15% federal government
- 6% private

In 2016, FSAP processed 86 registration renewals (19 AgSAS and 67 DSAT). Three entities applied to FSAP for new registrations, two for AgSAS and one for DSAT. One AgSAS application was approved, and the other two remained pending at the start of 2017. Sixteen entities withdrew from FSAP: fourteen from DSAT and two from AgSAS. One academic entity transferred their registration from AgSAS to DSAT and was not included in the totals for new applications or entity withdrawals.

## Security Risk Assessments

A security risk assessment (SRA) is an electronic records check performed by the Federal Bureau of Investigation's (FBI) Criminal Justice Information Services Division (CJIS) to determine whether a person requesting to have access to select agents and toxins is a "restricted person"<sup>1</sup> or otherwise may be prohibited from having such access. CJIS conducted 3,798 SRAs in 2016, with 10 individuals identified as meeting the definition of a "restricted person."

## Inspections

FSAP conducted 181 inspections in 2016. FSAP conducts several types of inspections of registered entities, such as: a registration renewal, an incident or report that indicates a possible lack of compliance with the select agent regulations (SAR),<sup>2</sup> periodic verifications that an entity has made corrective actions identified during previous inspections, the addition of new space, and a new registration application. Of the 181 inspections, 29 were conducted by AgSAS alone, 103 were conducted by DSAT alone, and 49 inspections were conducted jointly. Inspection length ranged from 1 to 8 federal government business days with inspectors on-site for an average length of 3 days.

## Inspection Findings and Compliance

FSAP works closely with all regulated entities to ensure that they are complying with the SAR. Inspection findings range from minor documentation errors in plans to serious biosafety or security issues, such as failure to use personal protective equipment (PPE) appropriately or working with a select agent outside of approved registered laboratory spaces.

When an inspector finds a significant biosafety and/or security concern during an inspection, FSAP works with the entity to bring it into compliance with the SAR. In some cases, an entity is offered the opportunity to participate in the FSAP Corrective Action Plan (CAP) program, in which the entity develops and implements a plan of corrective actions closely monitored by FSAP. If an entity chooses not to participate in the CAP program, the entity is expected to successfully resolve the regulatory departures within 30 calendar days from the date of their inspection report. FSAP has the authority to suspend an entity's registration, in part or in whole, when a departure from the SAR is found to represent a danger to human, animal, or plant health, or to public safety.<sup>3</sup> An entity may also be referred to the United States Department of Health and Human Services (HHS) Office of Inspector General (OIG) or APHIS Investigative and Enforcement Services (IES) for further investigation and possible civil penalties. FSAP can also notify the FBI of inspection findings that may involve a violation of criminal law.

In 2016:

- Five entities agreed to participate in the CAP program.
- Three entities had their registration suspended.
- Three entities were referred to either the HHS OIG or USDA IES.
- FBI was notified of twelve matters.

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<sup>1</sup> The definition of a "restricted person" may be found in 18 U.S.C. § 175b(d).

<sup>2</sup> The select agent regulations can be found at 7 C.F.R. Part 331, 9 C.F.R. Part 121, and 42 C.F.R. Part 73.

<sup>3</sup> Criteria for registration suspension is found in section 8 of 7 C.F.R. Part 331, 9 C.F.R. Part 121, and 42 C.F.R. Part 73.

## Confidential Reporting Systems

HHS OIG, USDA OIG, and FSAP operate confidential systems for individuals to report biosafety and security issues associated with the possession, use, and transfer of BSAT. Each report received is investigated to determine if a violation of the regulations has occurred. FSAP received two such reports in 2016. As a result of one report, an entity was suspended and a referral was made to HHS OIG. No actions were taken in relation to the second report because FSAP inspectors were unable to confirm the allegations.

## Restricted Experiments

An individual or entity may not conduct or possess products resulting from restricted experiments involving BSAT unless approved by and conducted in accordance with the conditions prescribed by FSAP. The SAR define two types of restricted experiments:

1. The deliberate transfer of, or selection for, drug resistance traits to select agents that are not known to acquire the trait naturally, if such acquisition could compromise the control of disease agents in humans, veterinary medicine, or agriculture.
2. The deliberate formation of synthetic or recombinant DNA containing genes for the biosynthesis of select toxins lethal for vertebrates at an  $LD_{50} < 100$  ng/kg body weight.<sup>4</sup>

In 2016, FSAP received six restricted experiment requests that met the restricted experiment definition. One request was to generate nucleic acids encoding for botulinum neurotoxin and was approved. Three requests were for the transfer of drug resistance traits and were denied. The remaining two restricted experiment requests were still pending as of December 31, 2016. In 2016, FSAP received 38 requests that did not meet the definition of a restricted experiment and therefore did not require approval of FSAP.

## Exclusions

An entity or individual may request to exclude from the SAR an attenuated strain of a select agent or a select toxin modified to be less potent or toxic. In 2016, DSAT received three requests to exclude attenuated select agent strains or less potent/toxic forms of select toxins. All three DSAT requests were approved. AgSAS received one exclusion request, which was denied due to insufficient data to demonstrate attenuation.

## Report of the Identification of a Select Agent or Toxin

The [Report of the Identification of a Select Agent or Toxin](#) (APHIS/CDC Form 4) is used by registered entities and unregistered clinical, diagnostic, or public health laboratories to notify FSAP of BSAT identified as a result of diagnosis, verification, and proficiency testing, and of the final disposition of identified BSAT. Unregistered laboratories may encounter BSAT in the course of their diagnostic activity. When this occurs, the laboratory is required to submit an APHIS/CDC Form 4 and either register with FSAP to keep the sample, transfer the sample to an entity registered to possess that BSAT, or destroy the sample.

FSAP received 1,096 APHIS/CDC Form 4s in 2016: AgSAS received 66 APHIS/CDC Form 4s while DSAT received 1,030.

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<sup>4</sup> Lethal dose 50 ( $LD_{50}$ ) refers to the amount of toxin (ng) required to kill 50% of the animals exposed to the toxin as a function of the body weight of the animal (kg). Currently, only nucleic acids containing genes for the biosynthesis of Botulinum neurotoxin meet the definition of 42 CFR 73.13 (b)(2).

The top 10 most identified BSAT reported to DSAT in 2016 were: Botulinum neurotoxin (237)<sup>5</sup>, Botulinum producing species of *Clostridium* (163), *Francisella tularensis* (160), *Brucella melitensis* (100), *Brucella abortus* (81), Eastern equine encephalitis virus (73), *Brucella suis* (70), *Yersinia pestis* (51), *Coxiella burnetii* (46), and *Burkholderia pseudomallei* (12).

The top 6 identified BSAT reported to AgSAS in 2016 were: Newcastle disease virus (30), *Ralstonia solanacearum* (18), Highly pathogenic avian influenza virus (8), African swine fever virus (3), Foot-and-mouth disease virus (3), and Rift Valley fever virus (3).

## Transfers of Select Agents or Toxins

The [Request to Transfer Select Agents and Toxins](#) (APHIS/CDC Form 2) is used by entities to request prior authorization to transfer BSAT. BSAT may be transferred from one entity to another for purposes including additional testing of diagnostic specimens that have been identified to contain a select agent or toxin, scientific or clinical research, and production of therapeutics. In 2016, FSAP approved 260 transfers, 188 by DSAT and 72 by AgSAS, including 31 DSAT and 47 AgSAS importations.

## Theft, Loss, and Release of Select Agents and Toxins

The [Incident Form to Report Potential Theft, Loss, Release, or Occupational Exposure](#) (APHIS/CDC Form 3) is used by entities to report a BSAT theft, loss, or release. An individual or entity is required by the SAR (7 CFR § 331.19, 9 CFR § 121.19, and 42 CFR § 73.19) to notify FSAP immediately upon discovery of a theft (unauthorized removal of BSAT), loss (failure to account for BSAT), or release (occupational exposure or release of BSAT outside of the primary barriers of the biocontainment area). An individual or entity must immediately notify FSAP of each theft, loss, and release, and appropriate federal, state, or local law enforcement agencies for thefts and losses. All thefts or losses must be reported, even if the BSAT is subsequently recovered and/or the responsible parties are identified. For each theft, loss, or release, an APHIS/CDC Form 3 must be submitted to FSAP within 7 calendar days.

In 2016, FSAP received 196 APHIS/CDC Form 3 reports of releases and 9 APHIS/CDC Form 3 reports of losses.

- Of the 196 reports of release, 177 were determined to represent potential occupational exposure to laboratory workers. The remaining 19 reports were associated solely with release outside of containment with no associated occupational exposure. Of the 177 potential exposure reports, 44% (78) originated from entities registered with FSAP, while 56% (99) were submitted by unregistered entities.
- The FBI was notified on eight of the nine APHIS/CDC Form 3 reports of losses, and it investigated all eight losses. The FBI was not notified about one of the nine losses because the entity recovered the select agent. The FBI determined that there was no criminal nexus in any of the eight cases of losses it investigated.

None of the releases resulted in illnesses, deaths, or transmissions among workers or outside of laboratories into the surrounding environment. No thefts of BSAT were reported in 2016.

## Emergency Response

FSAP reaches out to assist entities with transferring or securing BSAT that may be impacted by adverse weather events that could affect the safety and security of BSAT. FSAP assistance includes arranging transfers and/or destruction of BSAT. FSAP tracked 14 adverse weather events in 2016. FSAP successfully contacted a total of 86

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<sup>5</sup> Infant Botulism cases represent ~80% of botulism cases every year. [CDC National Botulism Surveillance website](#).

affected entities, none of which required assistance. There were no reported thefts, losses, or releases of BSAT associated with weather events.

## **Federal Register Notices, Policy Statements, Guidance, and Public Comment**

In 2016, FSAP issued numerous Federal Register notices, policies, guidance, and requests for public comment. Some examples of the 2016 FSAP issuances include:

- Advance notice of proposed rulemaking for the biennial review and republication of the list of [HHS](#) (81 FR 2805, January 19, 2016) and [USDA](#) (81 FR 2762, January 19, 2016) select agents and toxins
- [Publication of Interim Final Rule](#) - *B. cereus* Biovar *anthracis* (81 FR 63138, September 14, 2016)
- Revised policy statement regarding the inactivation of *Bacillus anthracis*
- Revised Select Toxin Guidance Document
- Revised Guidance on Drills and Exercises
- New Inspection Report Dispute Process

## **Outreach**

FSAP has an active outreach program designed to provide opportunities for interaction between FSAP and members of the regulated community. Outreach initiatives in 2016 included exhibiting an informational booth at scientific conferences to provide guidance and promote compliance with the SAR, a one-day workshop for FSAP-approved users to share best practices, and a multi-day in-person workshop for Responsible Officials.<sup>6</sup>

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<sup>6</sup> A Responsible Official (RO) is the individual designated by an entity to have the authority and control to ensure compliance with the Select Agent Regulations. The role of the RO is independent of the organizational structure at the entity.

## Acronyms

Acronym	Meaning
AgSAS	Agriculture Select Agent Services
Ag-ISATTAC	Agricultural-Intragovernmental Select Agents and Toxins Technical Advisory Committee
APHIS	Animal and Plant Health Inspection Service
ASM	American Society for Microbiology
BSAT	Biological Select Agents and Toxins
BSC	Biosafety Cabinet
BSL	Biosafety Level
CAP	Corrective Action Plan
CDC	Centers for Disease Control and Prevention
CJIS	Criminal Justice Information Services Division
DSAT	Division of Select Agents and Toxins
FAQ	Frequently Asked Questions
FBI	Federal Bureau of Investigation
FESAP	Federal Experts Security Advisory Panel
FSAP	Federal Select Agent Program
FTAC-SAR	Fast Track Action Committee on Select Agent Regulations
HHS	United States Department of Health and Human Services
IES	Investigative and Enforcement Services
ISATTAC	Intragovernmental Select Agents and Toxins Technical Advisory Committee
NIH	National Institutes of Health
OIG	Office of Inspector General
RO	Responsible Official
PPE	Personal Protective Equipment
PPQ	Plant Protection and Quarantine
SAR	Select Agents and Toxins Regulations
SRA	Security Risk Assessment
TLR	Theft, Loss, or Release
USDA	United States Department of Agriculture
USG	United States Government
VS	Veterinary Services



## Introduction

The Federal Select Agent Program (FSAP) is jointly managed by the Department of Health and Human Services (HHS), Centers for Disease Control and Prevention (CDC)/Division of Select Agents and Toxins (DSAT) and the Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS)/Agriculture Select Agent Services (AgSAS). Together, FSAP oversees the possession, use and transfer of biological select agents and toxins (BSAT), which have the potential to pose a severe threat to human, animal or plant health or to animal or plant products in accordance with the HHS and USDA select agent and toxin regulations (42 CFR Part 73, 7 CFR Part 331, and 9 CFR Part 121) (SAR). FSAP helps to ensure work with BSAT is conducted as safely and securely as possible by:

- Developing, implementing, and enforcing the select agent regulations (SAR).
- Maintaining a national database to track where and what work is being conducted with BSAT.
- Inspecting entities that possess, use, or transfer BSAT to ensure that legitimate use efforts are conducted safely and securely.
- Ensuring that all individuals who have access to BSAT undergo a security risk assessment (SRA) performed by the Federal Bureau of Investigation (FBI)/Criminal Justice Information Services Division (CJIS).
- Developing guidance documents and conducting informational workshops and webinars to help regulated entities maintain SAR compliance.
- Investigating incidents in which non-compliance with the SAR may have occurred.

In 2015, the United States Government published three reports that included recommendations to strengthen the government's safety and security practices and the oversight system, both through FSAP and at a broader national level. One of the reports was developed by a federal advisory panel, the [Federal Experts Security Advisory Panel \(FESAP\)](#). A second report was informed by external stakeholder input, and developed by the [Fast Track Action Committee on Select Agent Regulations \(FTAC-SAR\)](#). CDC published a third report containing recommendations to improve the CDC select agent and toxin regulatory program, the [90-day Internal Review of the Division of Select Agents and Toxins](#). There are many recommendations across the three reports that complement one another and that seek to support the same focus area. FSAP has implemented most of the recommendations and has provided periodic progress updates online, which will help to strengthen biosafety and security practices and oversight, and further ensure compliance with the SAR.

This report marks the program's second annual effort towards communicating operational metrics to the public to further public understanding of FSAP. FSAP will continue to publish a similar report on an annual basis.

The following report summarizes calendar year 2016 data for FSAP.

## Key Program Statistics

### Registration

#### Registered Entities

BSAT are divided into four categories based on whether the agent causes disease in humans, animals, or plants. In accordance with Sections 201 and 212(a)(2) of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (Pub. L. 107-188), FSAP performs biennial reviews to update and revise the list of BSAT as necessary. The four categories of BSAT are:

- **HHS select agents and toxins** (42 CFR Part 73): BSAT that have the potential to pose a severe threat to public health and safety and are regulated by HHS.

- **Overlap select agents and toxins** (42 CFR Part 73 and 9 CFR Part 121): BSAT that have the potential to pose a severe threat to public health and safety and to animal health, or to animal products. Overlap BSAT are regulated jointly by USDA and HHS.
- **USDA Veterinary Services (VS) select agents and toxins** (9 CFR Part 121): BSAT that have the potential to pose a severe threat to animal health or to animal products and are regulated by USDA.
- **USDA Plant Protection and Quarantine (PPQ) select agents and toxins** (7 CFR Part 331): BSAT that have the potential to pose a severe threat to plant health or to plant products and are regulated by USDA.

Entities that wish to possess, use, or transfer BSAT must register with either DSAT or AgSAS by completing the [Application for Registration for Possession, Use, and Transfer of Select Agents and Toxins](#) (APHIS/CDC Form 1). An entity that plans to register for HHS-only BSAT must submit their APHIS/CDC Form 1 to DSAT. If the entity registers for USDA-only BSAT, it must register with AgSAS. If the entity plans to register for overlap BSAT or a combination of HHS-only and USDA-only BSAT, it may choose to register with DSAT or AgSAS. DSAT and AgSAS work together to jointly oversee entities that have BSAT under the other's authority.

APHIS/CDC Form 1 requires:

- Facility information.
- A list of BSAT to be possessed, used, or transferred by the entity.
- A list of individuals who will have access to BSAT.
- A description of the work to be performed.
- Information about where the work will be performed.

Registration with FSAP requires an entity to renew their registration at least every 3 years.

Once the initial APHIS/CDC Form 1 is received, it is reviewed and a file manager is assigned to the entity. A site inspection is then scheduled to verify information submitted on the APHIS/CDC Form 1 and to review the site-specific biosafety and security measures are in place. Once the inspection is completed and any issues identified have been addressed, the entity receives a certificate of registration, which allows the entity to acquire and work with BSAT.

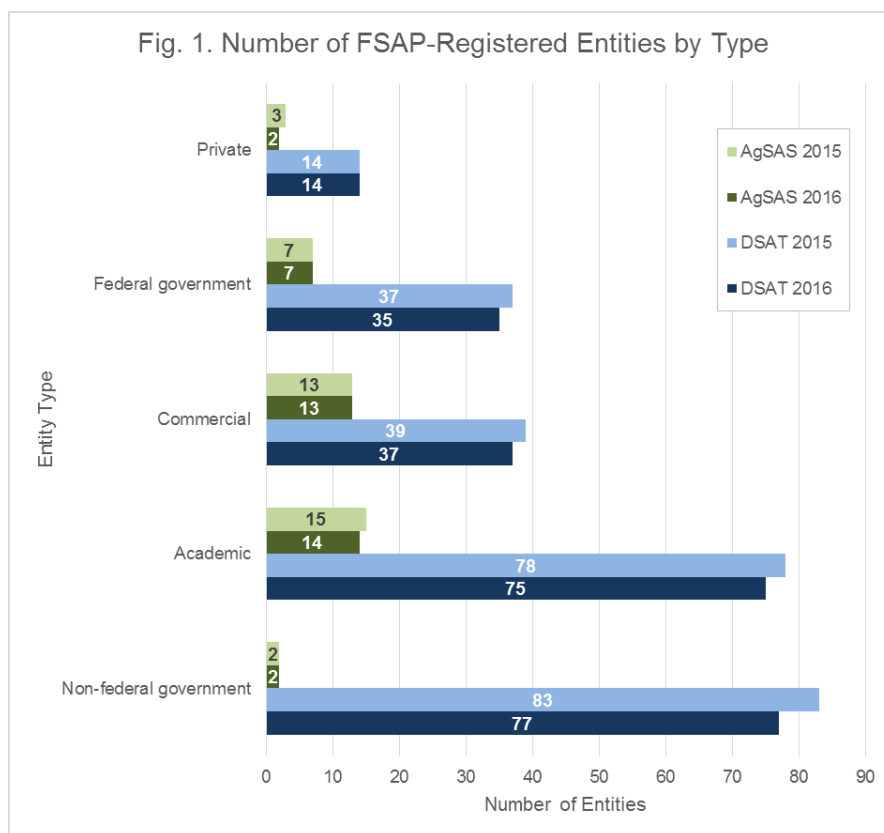
FSAP regulates a diverse community of entities ranging from government facilities at the federal, state, and local levels, to academic institutions, commercial, and other private entities in the United States. Work with BSAT includes: clinical diagnostics that are critical to inform patient care decisions, disease surveillance and confirmation services, basic science and clinical research, and production of biologics and therapeutics such as antibiotics and vaccines.

Registered entities can be sorted into five types:

- **Academic** – A university, college, or other institution of higher learning. Academic institutions can be either private (neither owned nor controlled by any government entity) or state (predominantly funded through the government).
- **Commercial** – A privately owned for-profit company including partnerships and corporations either privately held or whose shares are traded on the open market.
- **Federal government** – An entity that is part of an agency of the federal government.

- **Non-federal government** – An entity that is part of an agency of a state or local government (excluding academic entities).
- **Private** – A privately owned company including partnerships and corporations where no part of the income is distributed to its owners, directors, officers, members, or stockholders and whose principal purpose is for charitable or benevolent purposes.

At the end of 2016, 276 entities were registered with FSAP, including 238 with DSAT and 38 with AgSAS (Figure 1), which represents a 5% reduction from 2015 (data not shown). One entity transferred their registration from AgSAS to DSAT. The number of entity types registered with each agency either reduced or remained unchanged during 2016. Of the 276 entities, 32% were registered as an academic entity, followed by 29% as non-federal government, 18% commercial, 15% federal government, and 6% private, which is consistent with the 2015 data (data not shown).



The lead agency, DSAT or AgSAS is responsible for coordinating all activities and communications with respect to an entity’s registration, including coordination with the non-lead agency for entities with overlap agents. In 2016, 51 entities were jointly overseen by AgSAS and DSAT: AgSAS served as the lead agency for 14 entities and DSAT served as the lead agency for 37 entities. Compared to 2015, the number of jointly overseen entities led by DSAT increased by one in 2016 while the number led by AgSAS reduced by one entity.

### New Registrations

A facility must register with FSAP to possess, use, or transfer BSAT. In 2016, FSAP received three new applications requesting to register to possess, use, or transfer BSAT: two for AgSAS and one for DSAT. AgSAS approved one application from a federal government entity. AgSAS and DSAT each were in receipt of one application that was not completed during 2016 and were pending at the start of 2017. By comparison, AgSAS and DSAT each approved two new registrations in 2015.

## Renewals

Registered entities must renew their registration at least every 3 years. To renew a registration, an entity must submit an updated APHIS/CDC Form 1 and undergo a renewal inspection. In 2016, AgSAS approved 19 and DSAT approved 67 registration renewals, for a total of 86 renewals. By comparison, AgSAS approved 12 and DSAT approved 92 registration renewals in 2015. It is important to note that the registration renewal is based on the original registration date.

## Entity Withdrawals

When an entity decides that it no longer needs to possess, use, or transfer BSAT, it can request to withdraw its registration from FSAP. To do so, the entity must provide documentation that all of the BSAT in its possession was either destroyed or transferred to another registered entity via an approved APHIS/CDC Form 2. If the entity decides to resume BSAT work after withdrawing their registration, it must reapply to obtain a new FSAP certificate of registration. As shown in Table 1, 16 entities withdrew their registration from FSAP in 2016: 14 entities from DSAT and 2 entities from AgSAS. Eleven fewer entities withdrew their registration from FSAP in 2016 than in 2015. The reasons entities cited for withdrawing were similar in 2015 and 2016, which were primarily that they no longer needed to work with BSAT.

Table 1. Number of entity withdrawals by agency and entity type, 2016

Entity Type	AgSAS	DSAT
Academic		3
Commercial	1	3
Federal government	1	2
Non-federal government		6

## Tier 1 BSAT

Tier 1 BSAT are those that represent the greatest risk of deliberate misuse with the most significant potential for mass casualties or devastating effects on the economy, critical infrastructure, or public confidence. Twelve entities registered with AgSAS are registered for Tier 1 BSAT, representing 32% of all AgSAS-led entities, compared with 13 entities (33%) in 2015. One hundred and thirty entities registered with DSAT are registered for Tier 1 BSAT, representing 55% of all DSAT-led entities, compared with 135 entities (54 %) reported for 2015. The total percentage of FSAP-regulated entities registered for Tier 1 BSAT remained unchanged at 51%.

51% of all FSAP-regulated entities are registered for Tier 1 BSAT.

## *Bacillus cereus* Biovar *anthracis*

### Entities registered for *Bacillus cereus* Biovar *anthracis*

On September 14, 2016, DSAT added *Bacillus cereus* Biovar *anthracis* to the list of select agents and toxins as an HHS-only Tier 1 BSAT because it has virulence properties similar to *B. anthracis* (also regulated as a Tier 1 BSAT). The SAR requirements for *B. cereus* Biovar *anthracis* were effective on October 14, 2016. Currently, two federal government entities have submitted amendments to their registration to add *B. cereus* Biovar *anthracis*. The amendment for one entity has been approved while the other amendment is pending as of the start of 2017. Each entity was already registered for Tier 1 BSAT, so the addition of *B. cereus* Biovar *anthracis* to their registrations did not affect the number of entities registered with FSAP as Tier 1.

## Inactivated *Bacillus anthracis* and *Bacillus cereus* Biovar *anthracis*

### Waivers for inactivated *Bacillus anthracis* and *Bacillus cereus* Biovar *anthracis* material

In June 2015, FSAP released its first policy outlining requirements for inactivating material containing regulated strains of *B. anthracis*. The policy applied to all entities possessing or producing this material. The policy included a provision to allow an entity to request a waiver from the policy requirements if the entity could demonstrate that the material was inactivated sufficiently. On September 30, 2016, FSAP revised the policy, with key changes including the following:

- Clarifies that the policy is also applicable to *B. anthracis* Pasteur strain and *B. cereus* Biovar *anthracis* (effective October 14, 2016).
- Updates the definition of safety margin.
- Removes the requirement for statistically defensible inactivation criteria until guidance can be provided but maintains the requirement that 100% of the inactivated sample must be used during procedure validation.
- Clarifies the neutralization step for chemically inactivated material.
- Clarifies the sample volume sections to include procedures for large volume cultures.
- Clarifies that to qualify for an exclusion an entity must maintain a permanent record of the validation data for the inactivation process being used.

In 2016, FSAP approved 14 of the 15 waiver requests. As shown in Table 2, waivers for blood products and nucleic acid preparations constituted the majority of the waivers reviewed. A liquid culture waiver request was denied due to the potential impact of chemical inactivation on viability testing and an inadequate viability testing protocol. FSAP did not receive any waiver requests for *B. cereus* Biovar *anthracis* material.

Table 2. Inactivated *B. anthracis* waivers processed by FSAP, 2016

Specimen Type	Approved*	Denied
Blood products (e.g., serum and plasma)	9	-
Nucleic acid extractions	4	-
Liquid culture	1	1
Gamma phage production	1	-

\* One approved waiver request included more than one specimen type

## Top 10 Agents Registered With Each Agency

Table 3 lists the top 10 agents registered by each agency in 2016. To determine the top 10 agents registered by each agency, FSAP counted the number of entities registered for each BSAT, regardless of the number of rooms registered for that BSAT at each facility. For example, if an entity has multiple rooms registered for the same BSAT, the BSAT is only counted once for that entity for this report.

**Table 3. Top 10 agents registered with each agency, 2016**

Registered with DSAT	Registered with AgSAS
1. <i>Brucella melitensis</i>	1. Newcastle disease virus
2. <i>Brucella suis</i>	2. Avian influenza virus
3. <i>Brucella abortus</i>	3. <i>Bacillus anthracis</i> *
4. <i>Bacillus anthracis</i> (Pasteur strain)	4. <i>Brucella abortus</i>
5. <i>Francisella tularensis</i> *	5. <i>Ralstonia solanacearum</i>
6. <i>Yersinia pestis</i> *	6. <i>Xanthomonas oryzae</i>
7. <i>Burkholderia pseudomallei</i> *	7. <i>Francisella tularensis</i> *
8. <i>Bacillus anthracis</i> *	8. <i>Yersinia pestis</i> *
9. <i>Burkholderia mallei</i> *	9. Eastern equine encephalitis virus
10. Botulinum producing species of <i>Clostridium</i> *	10. <i>Burkholderia pseudomallei</i> *

\* indicates Tier 1 agent or toxin

## Laboratory Types

Each regulated entity has one or more laboratories or secure storage location(s) where BSAT work is conducted or stored. Laboratories that work with BSAT range from biosafety level 2 (BSL-2) to maximum containment at biosafety level 4 (BSL-4). At each containment level, there is an equivalent set of biosafety guidelines for work with animals designated as animal biosafety level 2 (ABSL-2) through maximum containment at animal biosafety level 4 (ABSL-4). There is also a BSL-3Ag containment level which is generally used for work with agricultural animals in which the laboratory itself serves as primary containment. Primary containment refers to devices that protect the worker, product, and environment from exposure to microbiological agents, such as a biosafety cabinet (BSC).

In 2016, 32% of entities had registered ABSL-2/BSL-2 laboratories, 80% of entities were registered for BSAT work in ABSL-3/BSL-3 laboratories, and 3% of entities have registered ABSL-4/BSL-4 laboratories. Entities may register multiple types of BSL laboratories at their facility, depending on the work required in those laboratories. Please note that the ABSL-3/BSL-3 entity type percentages do not add up to 100% due to rounding decimals to the nearest whole number.

- Of the entities that have ABSL-2/BSL-2 laboratories, 60% were registered for Tier 1 BSAT. Thirty-two percent of these entities were commercial, 24% were federal government, 22% were academic, 12% were non-federal government, and 10% were private.
- Of the entities that have ABSL-3/BSL-3 laboratories, 52% were registered for Tier 1 BSAT. Thirty-five percent of these entities were academic, 10% were commercial, 13% were federal government, 35% were non-federal government, and 6% were private.
- Of the entities that have ABSL-4/BSL-4 laboratories, 100% were registered for Tier 1 BSAT. Twenty-five percent of these entities were academic, 62.5% were federal government, and 12.5% were private.

## Security Risk Assessments

One of the fundamental elements of the SAR is to keep BSAT out of the possession of individuals who might intend to misuse them, such as bioterrorists. FSAP works closely with the FBI's CJIS to identify those individuals who are prohibited from access to BSAT because they are a "restricted person" as defined by section 175b of title 18, United States Code (USC). A security risk assessment (SRA) is a CJIS electronic records check to determine whether an entity (including the owner and/or controller of an entity), an individual who wishes to register to possess, use, or transfer BSAT, or an individual who has been identified by a registered entity as having a legitimate need to access BSAT, is a "restricted person" or meets one of the statutory restrictors which would either deny registration/access or limit access, respectively. The results of an SRA assist FSAP in determining whether an individual or entity may

possess, use, or transfer BSAT, or if an individual may be granted access to BSAT. An SRA is valid for a period not to exceed 3 years.

In 2016, based on the 3,798 individual FBI SRAs conducted by CJIS, FSAP approved 3,748 individuals to have access to BSAT. Ten individuals were identified as a “restricted person” and were denied access to BSAT. The other 40 individuals who were not approved for access to BSAT never completed the application process. In August 2016, the FSAP introduced a new process that allowed individuals to work at multiple registered entities under one SRA. Because an individual may be approved for access to BSAT at more than one entity, FSAP granted 3,982 approvals in 2016. The number of approved individuals in 2016 (Table 4) is 10% fewer than 2015 (data not shown). Similar to 2015, the majority of SRAs performed in 2016 were for individuals working at academic entities, followed by individuals working at federal government entities. The number of approved individuals decreased for each entity type in 2016 compared to 2015 (data not shown).

**Table 4: Total security risk assessments by entity type and approval status, 2016**

Entity Type	Newly Approved SRAs in 2016	Individuals Identified as Restricted in 2016	Total Currently Active SRA as of 12/31/2016
Federal government	1,166	3	2,956
Non-federal government	481	2	1,190
Commercial	506	2	1,171
Private	421	0	860
Academic	1,408	3	3,486
Total	3,982*	10	9,663

*\*The total number of individuals approved for access to BSAT per entity type is greater than the number of SRAs conducted because individuals can be approved at multiple entities based on one SRA.*

A “restricted person” cannot be granted access to BSAT. According to the U.S. Patriot Act (18 USC 175(b)), a “restricted person” is a person 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 one year.
- Is a fugitive from justice.
- Is an unlawful user of any controlled substance (as defined in section 102 of the Controlled Substances Act (21 USC § 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 as to which the Secretary of State, pursuant to section 6(j) of the Export Administration Act of 1979 (50 USC App. 2405(j)), section 620A of chapter 1 of part M of the Foreign Assistance Act of 1961 (22 USC § 2371), or section 40(d) of chapter 3 of the Arms Export Control Act (22 USC 2780(d)), has made a determination (that remains in effect) that such country has repeatedly provided support for acts of international terrorism.
- 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 (8 USC 1182(a)(3)(B)(vi)).

In addition, the FBI will notify FSAP when they identify an individual who is reasonably suspected by any Federal law enforcement or intelligence agency of the following:

- Committing a crime set forth in 18 USC 2332b(g)(5).
- Knowing involvement with an organization that engages in domestic or international terrorism (as defined in 18 USC § 2331) or with any other organization that engages in intentional crimes of violence.

- Being an agent of a foreign power (as defined in 50 USC § 1801).

**Table 5. Number of “restricted person” categories by prohibitor type for restricted persons identified in 2016**

Prohibitor	Total*
Conviction exceeds 1 year (Has been convicted in any court of a crime punishable by imprisonment for a term exceeding one year)	7
An alien illegally or unlawfully in the United States	1
Fugitive from justice	1
Under indictment (Is under indictment for a crime punishable by imprisonment for a term exceeding one year)	1
Unlawful user of any controlled substance	1
<b>Total</b>	<b>11</b>

\* Total number of prohibitors is greater than the number of restricted persons since a person may have more than one prohibitor.

## Inspection Data

### Inspections

Entities regulated by FSAP are subject to announced and unannounced inspections. The type of inspection scheduled depends on the triggering event, but all inspections focus on the biosafety and security of the work with BSAT. The following are the types of inspections conducted by FSAP and their definitions:

- **Compliance** – Review of entity program for compliance issues, including inspections to investigate whistleblower reports.
- **Maximum containment** – Review of entity program, including laboratory spaces and documents, for ABSL-4 and BSL-4 laboratories.
- **New entity** – Review of all laboratory spaces and documents for an entity that is submitting a new application.
- **New space** – Review of laboratory space and documents for adding new laboratory space to an existing registration.
- **Renewals** – Review of entire entity program, including all registered spaces and documents, to renew existing registration, which are typically conducted every 3 years.
- **Verification** – Review of selected portions of the entity program, including assessment of responses to previous inspection departures, which are conducted within 12 to 18 months of a renewal inspection.

Inspections can be led by DSAT or AgSAS depending on the agents the entity is registered to possess, use, or transfer. DSAT inspects entities registered for HHS-only agents, and AgSAS inspects entities with USDA-only agents. Entities registered for both HHS and USDA agents are normally inspected jointly by DSAT and AgSAS. When joint inspection is not possible, each agency has agreed to recognize the other’s findings.

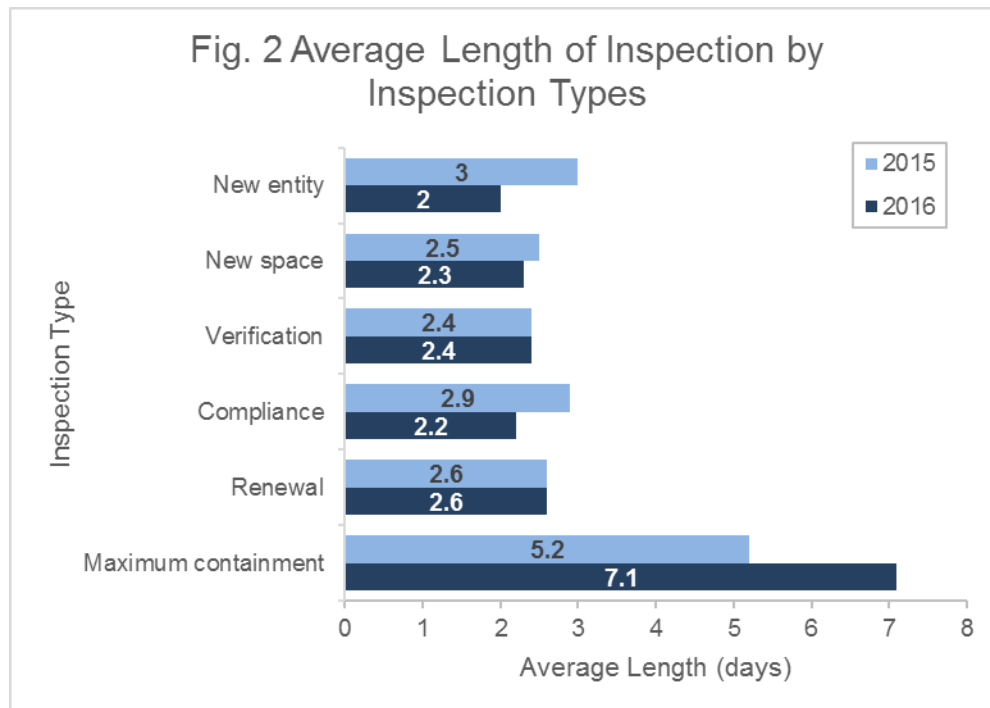
In 2016, FSAP performed 181 inspections: 29 by AgSAS, 103 by DSAT, and 49 jointly. By comparison, FSAP performed 216 inspections in 2015: 33 by AgSAS, 145 by DSAT, and 38 jointly, representing a 15% decrease in the number of FSAP inspections. The decreased number of inspections in 2016 may be due to a variety of factors such as, entity renewal cycle, decrease in the number of entities currently registered, and reductions in the number of fully trained FSAP inspectors.

### Length of Inspections

In 2016, inspection length ranged from 1 to 8 federal government business days on-site with an average length of 3 days, which was the same range and average for 2015. Figure 2 compares the 2015 and 2016 average length of an



FSAP inspection by inspection type. In both 2015 and 2016, maximum containment inspections were the longest inspections, likely due to the complexity of high containment facilities. In 2016, the average length of maximum containment inspections increased by almost 2 federal government business days due to a shortage of inspectors trained to conduct ABSL-4/BSL-4 inspections.



## Inspection Findings and Compliance

The goal of the SAR is to ensure a registered entity has the operating conditions to minimize biosafety and security risks. FSAP works closely with all regulated entities to assist them with SAR compliance. The following is a representative listing of the types of observations made by inspectors during inspections in 2016. These observations are not listed in any particular order.

- Omission or clarification needed in entity biosafety, incident response, or security plans.
- Inaccurate records for inventory, training, or access to BSAT.
- Biosafety practices not adequate to contain BSAT.
- Failure of Responsible Official (RO) to ensure adequate oversight of BSAT activities.
- Failure to properly implement all regulatory requirements for possession of Tier 1 BSAT.
- Failure to wear or use appropriate Personal Protective Equipment (PPE) in BSAT laboratories.
- Failure to properly secure BSAT materials from unapproved access.
- Work with BSAT materials outside of registered laboratories.
- Work with BSAT outside of a BSC.

## Corrective Action Plan

In March 2008, FSAP established the Corrective Action Plan (CAP) program to assist entities identified as having systemic biosafety and security deficiencies in achieving compliance with the SAR. To participate, an entity submits a detailed plan, including target completion dates and the specifics of how the entity will correct identified regulatory deficiencies. An entity's participation in the CAP program allows FSAP to provide technical assistance as well as monitor an entity's progress in correcting security or biosafety shortcomings. Participation in the CAP program is

voluntary. If an entity chooses not to use a CAP, the entity is expected to successfully resolve the regulatory departures identified in their inspection report process within 30 days.

In 2016, two AgSAS entities (one federal government and one commercial entity) and three DSAT entities (two academic and one non-federal government) agreed to participate in the CAP program. None of the entities that were offered participation in the CAP program declined. The five entities participating in the CAP program in 2016 were not in the CAP program in 2015. By comparison, six DSAT entities participated in the CAP program in 2015 while no AgSAS entities participated. At the end of 2016, one entity from 2015 and four entities from 2016 were still participating in the CAP program. Each CAP is unique, and FSAP carefully monitors and assists these entities to return to full compliance expeditiously.

Participants in the CAP program were each found to have one or more of the following types of systemic biosafety and security deficiencies:

- Had multiple incidents involving an entity's effluent decontamination system.
- Worked with BSAT in laboratories not listed on the entity's registration.
- Failed to follow safe work practices and work safely in an environment with BSAT that could have resulted in an occupational exposure to the BSAT (e.g., worked with viable BSAT outside of primary containment).
- RO failed to ensure compliance of the SAR for work with BSAT.
- Had inaccurate BSAT inventory records.
- Failed to secure BSAT properly which made the inventory vulnerable to theft.

**In 2016, five entities participated in the CAP program, representing less than 2% of all entities.**

### **Registration Suspensions**

An entity's registration can be suspended when a departure from the SAR is found to represent a danger to human, animal, or plant health, or to public safety.<sup>7</sup> An entity's registration remains suspended until the compliance issues are properly addressed. In 2016, three entities were suspended (one academic, one commercial, and one federal government), which is the same number of entities for 2015. The three entities were suspended in 2016 for the following reasons:

- Failure to 1) provide adequate Responsible Official oversight of program and 2) conduct and document due diligence for transfers of select toxins.
- Failure to comply with the SAR, including significant biosafety, training, incident response, record keeping, and Tier 1 regulatory departures noted during inspection.
- Failure to maintain a properly functioning effluent decontamination system.

None of the suspensions were appealed by entities in 2016.

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<sup>7</sup> Criteria for registration suspension is found in section 8 of 7 C.F.R. Part 331, 9 C.F.R. Part 121, and 42 C.F.R. Part 73.

## Reports and Referrals

### Confidential Reporting System

HHS Office of Inspector General (OIG), USDA OIG, and FSAP maintain confidential reporting systems that allow anyone to report safety, security, or other concerns associated with BSAT. FSAP received two reports for potential investigation in 2016, compared to three reports in 2015.

- A federal agency reported unauthorized transfers by a commercial entity of select toxin. Following a DSAT inspection, the entity was suspended and the matter was referred to the HHS OIG.
- A complaint received by AgSAS alleged that an academic entity was not safely working with an organism that could produce a select toxin. AgSAS and DSAT inspectors were unable to confirm the allegations.

### Referrals to HHS OIG or APHIS IES

Entities may be referred to HHS OIG or APHIS Investigative and Enforcement Services (IES) for further investigation and for civil monetary penalties for serious violations of the SAR. FSAP referrals to the HHS OIG or the APHIS IES reflect a serious departure from the SAR. FSAP referred three entities to HHS OIG or APHIS IES in 2016, compared with four entities in 2015.

- A commercial entity was referred to HHS OIG for the unauthorized transfers of a select toxin to an unregistered entity.
- An academic entity was referred to HHS OIG for failing to provide appropriate oversight of select agent activities and significant security, record keeping, and training departures noted during inspection.
- One referral to APHIS IES was a federal government entity that had a potential loss of a select agent that was identified during an inspection.

The 2016 referrals are still under investigation by HHS OIG or APHIS IES.

### FBI Notifications

Based on an agreement with the FBI, FSAP notifies the FBI of any security-related issue (for example, transfer of BSAT to an unregistered entity, allowing unapproved individuals access to BSAT, security breach of BSAT storage spaces, etc.) identified by a registered entity and any report of a loss of a select agent or toxin. This FSAP partnership with the FBI allows FSAP to leverage FBI resources to determine whether a security issue presents a criminal threat including whether a loss may have been a theft. FSAP also provides information in support of specific FBI investigations. In 2016, the FBI was informed of 12 matters for investigation. In all investigated cases, a FBI analysis determined there was no criminal nexus. In addition to the 12, one Form 3 was not investigated because the inventory was recovered.

- Eight matters concerned losses of BSAT. All losses were determined to be records management errors.
  - Six of the losses were initially reported to FSAP via APHIS/CDC Form 3.
  - The other two losses were notifications resulting from observations made during inspections, and subsequently reported via APHIS/CDC Form 3.
- Two matters concerned possible possession of select toxins. One notification concerned an unregistered entity that self-reported to DSAT. The second notification concerned an unregistered entity identified during an inspection of a registered entity.
- One matter concerned possible shipping violations.
- One matter concerned a possible falsification of inventory records.

## Restricted Experiments

An individual or entity may not conduct or possess products resulting from restricted experiments unless approved by and conducted in accordance with the conditions prescribed by FSAP. SAR defines two types of restricted experiments.

1. The deliberate transfer of, or selection for, drug-resistance traits to select agents that are not known to acquire the trait naturally, if such acquisition could compromise the control of disease agents in humans, veterinary medicine, or agriculture. (HHS-only, APHIS/VS-only, and Overlap agents)  
  
The deliberate transfer of, or selection for, a drug or chemical resistance trait to select agents that are not known to acquire the trait naturally, if such acquisition could compromise the control of disease agents in humans, veterinary medicine, or agriculture. (APHIS/PPQ-only agents)
2. The deliberate formation of synthetic or recombinant DNA containing genes for the biosynthesis of select toxins lethal for vertebrates at an LD<sub>50</sub> < 100 ng/kg body weight. Currently, only one select toxin (botulinum neurotoxin) possesses an LD<sub>50</sub> < 100 ng/kg body weight.

These experiments are considered restricted experiments due to their potential threat to human, animal or plant health, or to animal or plant products. FSAP review and approval of restricted experiments is required prior to the initiation of these studies.

FSAP has published a [Restricted Experiment Guidance Document](#) detailing instructions to entities and principal investigators on how to apply for review and approval of a proposed restricted experiment or appeal a decision made by FSAP.

The CDC Intragovernmental Select Agents and Toxins Technical Advisory Committee (ISATTAC) and Agriculture ISATTAC (Ag-ISATTAC) are tasked with reviewing the biosafety measures associated with proposed restricted experiments that could impact human health, or animal and plant health, respectively. Federal government departments including HHS (e.g., CDC, Federal Drug Administration, NIH), Department of Defense (DOD), Department of Homeland Security (DHS), and USDA participate in these committees. ISATTAC and Ag-ISATTAC also provide recommendations to the DSAT Director (for HHS and Overlap BSAT) and the AgSAS Director (for Overlap and USDA-only BSAT) on whether an experiment should be approved. Restricted experiments involving the deliberate introduction of a drug-resistant trait are reviewed to determine if the trait involves a drug used therapeutically for treatment. If the drug resistance trait could compromise the control of disease, other considerations are taken into account (e.g., whether there are other drugs available to treat the select agent infection, or whether the drug is used for treatment within or outside of the U.S.). Experiments with specific select agent strains that have naturally acquired resistance to drugs used to treat the disease are not considered restricted experiments.

Both restricted experiment types are assessed to ensure that the experiments are conducted safely under biosafety conditions that meet the biosafety guidelines prescribed in the CDC/NIH publication [Biosafety in Microbiological and Biomedical Laboratories 5th edition](#). In addition, FSAP ensures that entities address the [NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules](#) for restricted experiments involving these molecules.

**Experiments that meet the restricted experiment definition require written approval by FSAP before any work can begin.**

Restricted experiment approval decisions are the result of careful consideration of the unique situation at the entity, the work proposed by the principal investigator, biosafety factors, and the fact that BSAT cannot be transferred to another entity or principal investigator planning similar work without prior permission by FSAP.

As shown in Table 6, FSAP received six restricted experiment requests in 2016 that met the restricted experiment definition. DSAT received one restricted experiment request from a federal government entity for nucleic acids encoding for Botulinum neurotoxin, which was approved and three restricted experiment requests from an academic entity for the transfer of drug resistance traits into *B. abortus*, *B. melitensis*, and *B. suis*, which were denied. The remaining two restricted experiment requests are still pending as of December 31, 2016 and were received from an AgSAS-registered entity for transfer of drug resistance traits into *F. tularensis* and *Y. pestis*. In 2016, FSAP received 38 requests that did not meet the definition of a restricted experiment and therefore did not require approval from FSAP.

**Table 6: Summary of restricted experiments by entity type, select agent, and decision status, 2016**

Entity Type	Agent	Decision Status
Academic	<i>Brucella abortus</i>	Denied
Academic	<i>Brucella melitensis</i>	Denied
Academic	<i>Brucella suis</i>	Denied
Academic	<i>Francisella tularensis</i>	Pending
Academic	<i>Yersinia pestis</i>	Pending
Federal government	Botulinum Neurotoxin Nucleic Acids	Approved

## Exclusions

The SAR provides criteria for the exclusion of BSAT (See 42 CFR §§ 73.3 and 73.4, 9 CFR §§ 121.3 and 121.4, 7 CFR § 331.3). A discussion of the criteria can be found in the [Exclusion Guidance Document](#). An entity or individual may request to exclude from the SAR an attenuated (weakened) strain of a select agent or a select toxin modified to be less potent or toxic. Similar to restricted experiments, ISATTAC or Ag-ISATTAC review requests for exclusion and provides a recommendation to FSAP. As required by SAR, FSAP renders a written decision to the requestor and posts the exclusion on the FSAP website so that others can benefit from this knowledge in case they also wish to work with the attenuated strain or a toxin modified to be less potent or toxic.

In 2016, FSAP received four requests to exclude attenuated select agent strains or less potent/toxic forms of select toxins. Three of the four requests were approved and excluded based on results demonstrating they no longer pose a threat to public health and safety, animal health or animal products, and plant health or plant products (Table 7). A detailed list of all excluded select agent strains can be found at [Select Agents and Toxins Exclusions](#).

**Table 7. Summary of requests for exclusions by entity type, select agent, and approval status, 2016**

Entity Type	Select Agent	Decision Status
Academic	SEB single site mutant Q210A and SEC single site mutant N23A	Approved
Academic	$\Delta$ lpp $\Delta$ msb $\Delta$ ail <i>Yersinia pestis</i> CO92	Approved
Commercial	Foot-and-mouth disease virus	Denied due to insufficient data to demonstrate attenuation
Federal government	Catalytically inactivate BONT B, C, E, F	Approved

## Report of the Identification of a Select Agent or Toxin

Clinical, diagnostic, or public health laboratories<sup>8</sup> that do not deliberately work with BSAT may identify BSAT within a specimen or environmental sample. If the laboratory is not registered with FSAP, the laboratory is required to either register with FSAP to keep the sample, transfer the sample to an entity registered to possess that BSAT, or destroy the sample.

The Report of the Identification of a Select Agent or Toxin (APHIS/CDC Form 4) is used to notify FSAP of the identification of BSAT that is the result of diagnosis, verification, or proficiency testing, as well as the final disposition of the identified BSAT. FSAP has published a [Guidance Document for the Completion of APHIS/CDC Form 4](#) on the website. There are three versions of the APHIS/CDC Form 4 depending on the reporting circumstance:

- [APHIS/CDC Form 4A](#) – Reporting the Identification from a Clinical/Diagnostic Specimen
- [APHIS/CDC Form 4B](#) – Reporting the Identification from a Proficiency Test
- [APHIS/CDC Form 4C](#) – Federal Law Enforcement Reporting Seizure of Select Agent or Toxin

APHIS/CDC Forms 4A and 4B are used by institutions that need to report the identification of BSAT. APHIS/CDC Form 4C is used by law enforcement to notify FSAP of seized BSAT.

DSAT received and processed 1,030 APHIS/CDC Form 4s in 2016. The top 10 BSAT in 2016 identified on APHIS/CDC Form 4s were the same as 2015, although the order and number of APHIS/CDC Form 4s for each BSAT changed. Botulinum neurotoxin was the most common APHIS/CDC Form 4A for HHS or Overlap BSAT, followed by botulinum neurotoxin-producing species of *Clostridium* and *F. tularensis* (Table 8). By comparison, *F. tularensis* was the most common APHIS/CDC Form 4A in 2015. The number of *B. abortus* and *B. suis* APHIS/CDC Form 4As increased substantially in 2016 from 2015. Unregistered laboratories accounted for 17% of all reports of the identification of BSAT via APHIS/CDC Form 4A, in comparison to the 14% reported in 2015 (data not shown).

In addition to the APHIS/CDC 4A reports, DSAT received 15 APHIS/CDC Form 4B reports (5 for abrin, 2 for *B. anthracis*, 3 for *F. tularensis*, 3 for ricin, and 2 for *Y. pestis*). The reason for the small number of APHIS/CDC Form 4B reports is likely that the laboratories sponsoring proficiency testing typically use excluded BSAT which precludes the APHIS/CDC Form 4B reporting requirement. By comparison, abrin accounted for 14 of the 17 4B reports that DSAT received in 2015. DSAT did not receive any APHIS/CDC 4C reports in 2016, compared with three APHIS/CDC 4C reports in 2015.

AgSAS received and processed 66 APHIS/CDC Form 4A reports for USDA BSAT in 2016, including 30 reports of Newcastle disease virus, 18 reports of *R. solanacearum*, and 8 reports of avian influenza virus. The 2016 total is substantially less than 2015 due to the 263 reports of highly pathogenic avian influenza virus received by AgSAS from an outbreak in the spring and summer of 2015. The number of reports of Newcastle disease virus and *R. solanacearum* was relatively consistent from 2015 to 2016. AgSAS received one APHIS/CDC Form 4B for a report of Foot and Mouth Disease virus and no APHIS/CDC Form 4C reports. AgSAS did not receive any APHIS/CDC Form 4B or 4C reports in 2015.

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<sup>8</sup>To qualify for the exemption, clinical or diagnostic laboratories and other entities that have identified select agents contained in a sample presented for diagnosis, verification, or proficiency testing are required by the select agent regulations to report this identification to USDA or HHS by completing APHIS/CDC Form 4 - Report of the Identification of a Select Agent or Toxin. In addition to the reporting requirement, the identified select agent must be secured against theft, loss, or release during the period between identification and final disposition. In the event that a release has occurred, the laboratories must report this release using APHIS/CDC Form 3 - Report of Theft, Loss, or Release of a Select Agent or Toxin.

**Table 8. Top 10 BSAT Reported to DSAT on Form 4A by isolate type, 2016**

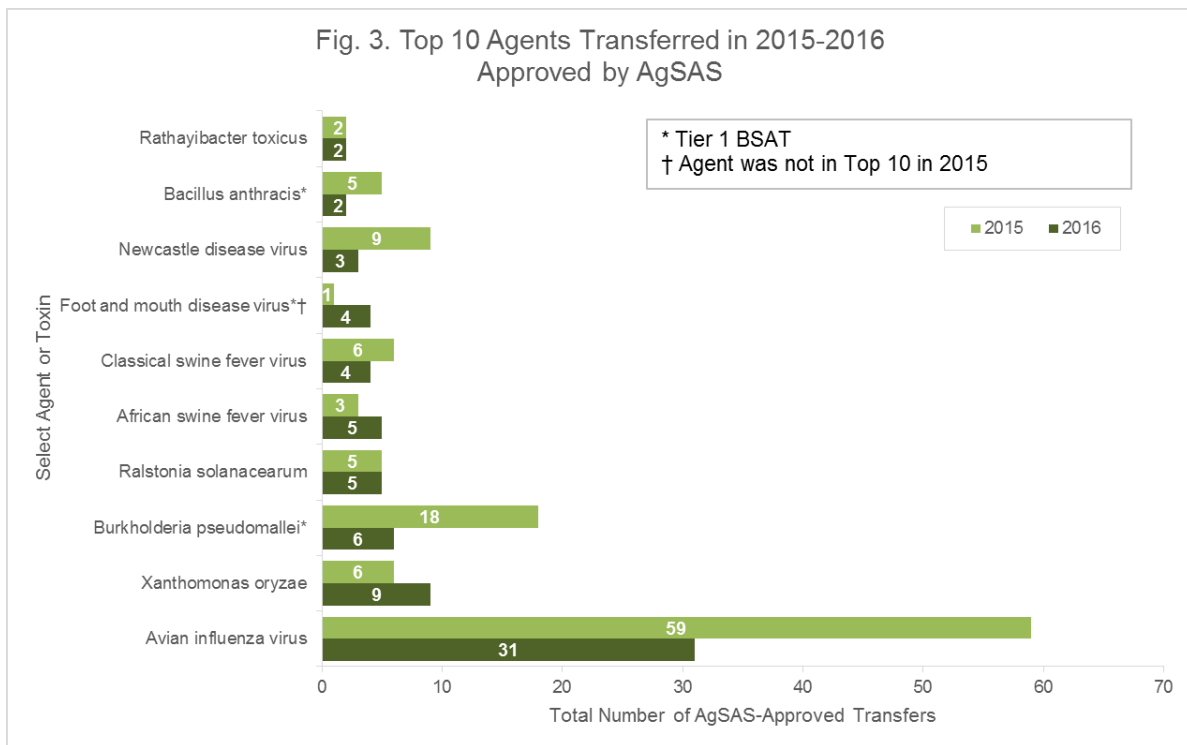
Agent/Toxin	Animal Specimens	Environmental Samples	Food Sample	Plant Specimens	Human Specimens	Total
Botulinum neurotoxins	55	1	7	0	174*	237
Botulinum neurotoxin producing species of <i>Clostridium</i>	48	0	5	1	110	164
<i>Francisella tularensis</i>	67	0	0	0	93	160
<i>Brucella melitensis</i>	1	0	2	0	97	100
<i>Brucella abortus</i>	77	0	0	0	4	81
Eastern Equine Encephalitis virus (Including genomic material)	48	23	0	0	2	73
<i>Brucella suis</i>	47	0	0	0	23	70
<i>Yersinia pestis</i>	46	0	0	0	4	50
<i>Coxiella burnetii</i>	35	0	0	0	13	48
<i>Burkholderia pseudomallei</i>	4	0	0	0	9	13
Total	428	24	14	1	529	996

\*Infant botulism cases represent ~80% of botulism case every year. For more information, please visit the [CDC National Botulism Surveillance website](#)

## Transfers of Select Agents or Toxins

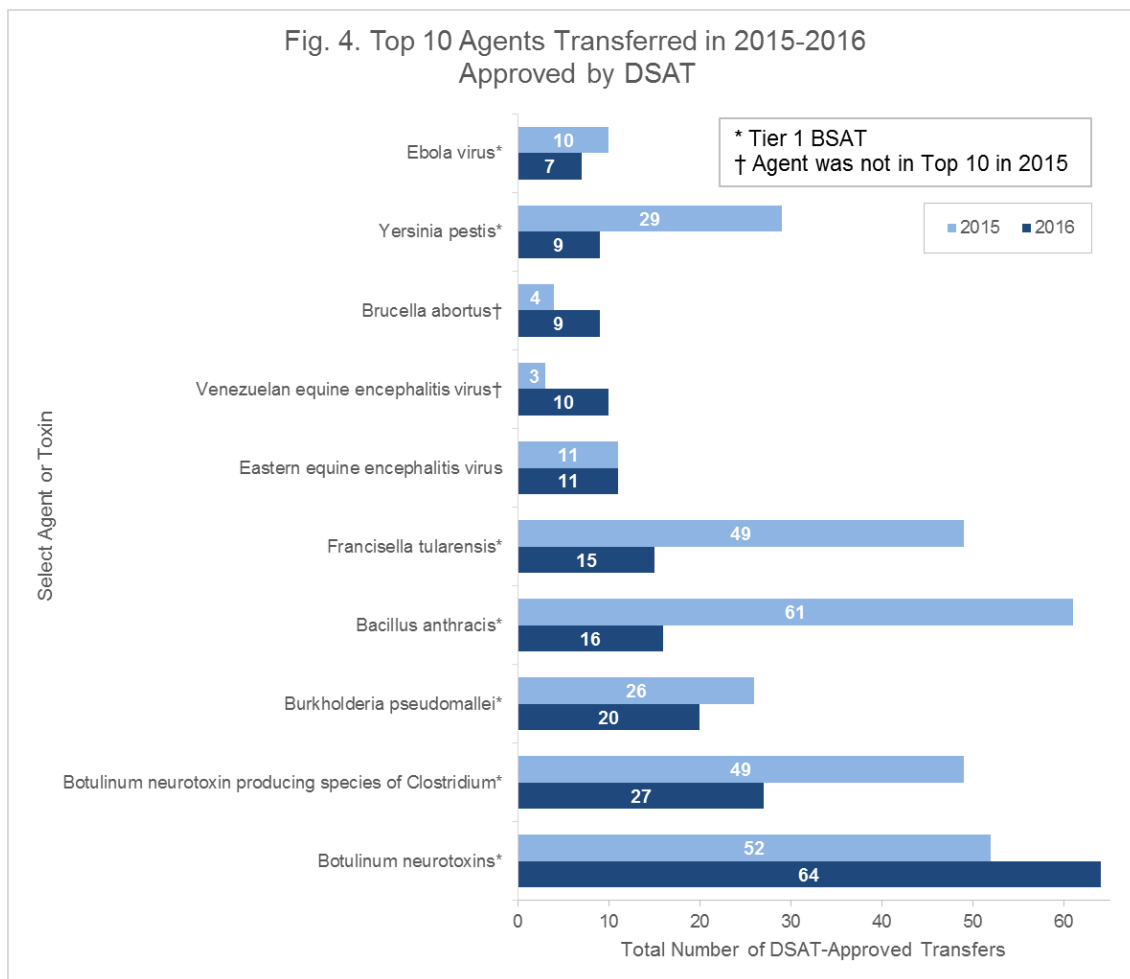
The Request to Transfer Select Agents and Toxins ([APHIS/CDC Form 2](#)) is used by entities to request authorization prior to transferring BSAT. BSAT may be transferred from one entity to another for diagnostic testing, scientific or clinical research, and production of therapeutics. FSAP has published an [APHIS/CDC Form 2 Guidance Document](#) and a [FAQ](#) to assist entities in requesting permission to transfer BSAT.

In 2016, FSAP approved 260 BSAT transfers, 72 by AgSAS and 188 by DSAT, a 44% decrease from 2015. The data suggests that there has been a downward trend in FSAP-approved transfers since 2012, with the exception of 2015. Thirty-eight percent of all BSAT were shipped from unregistered entities, an increase of 6% from 2015. Transfers from unregistered entities are mostly as a result of identification of BSAT in a diagnostic specimen.



AgSAS approved 54 fewer transfers in 2016 than 2015. Avian influenza virus was the most frequent AgSAS-approved transfer in 2015 and 2016, followed in 2016 by *Xanthomonas oryzae*, *B. pseudomallei*, African swine fever virus, and *R. solanacearum* (Figure 3). The number of avian influenza virus and *B. pseudomallei* transfers decreased substantially in 2016 while the number of transfers for other BSAT remained consistent compared to 2015. Of the 72 AgSAS approved transfers, 47 transfers were imported from outside the U.S.





DSAT approved 149 fewer BSAT transfers in 2016 than 2015. Botulinum neurotoxin was the most frequently approved BSAT transfer in 2016, followed by Botulinum neurotoxin-producing species of *Clostridium*, and *B. pseudomallei* (Figure 4). *B. anthracis*, which was the most frequent BSAT approved by DSAT for transfer in 2015, was the fourth most frequently approved BSAT transferred in 2016. In addition to *B. anthracis*, DSAT observed substantial decreases from 2015 in the number of approved transfers for *F. tularensis*, *Y. pestis*, and Botulinum neurotoxin-producing species of *Clostridium*. Conversely, DSAT observed slight increases in the number of approved transfers for Venezuelan equine encephalitis virus and *B. abortus*. Of the 188 DSAT-approved transfers in 2016, 31 transfers were imported from outside the U.S.

In 2016, 79 BSAT transfers were approved by FSAP for commercial entities, which was the most transfers approved for any entity type (Figure 5). The number of transfers approved for commercial and private entities was similar to 2015, as transfers approved for each entity type decreased by less than 20%. In contrast, the number of transfers approved for federal and non-federal government entities decreased by 48% and 92%, respectively.

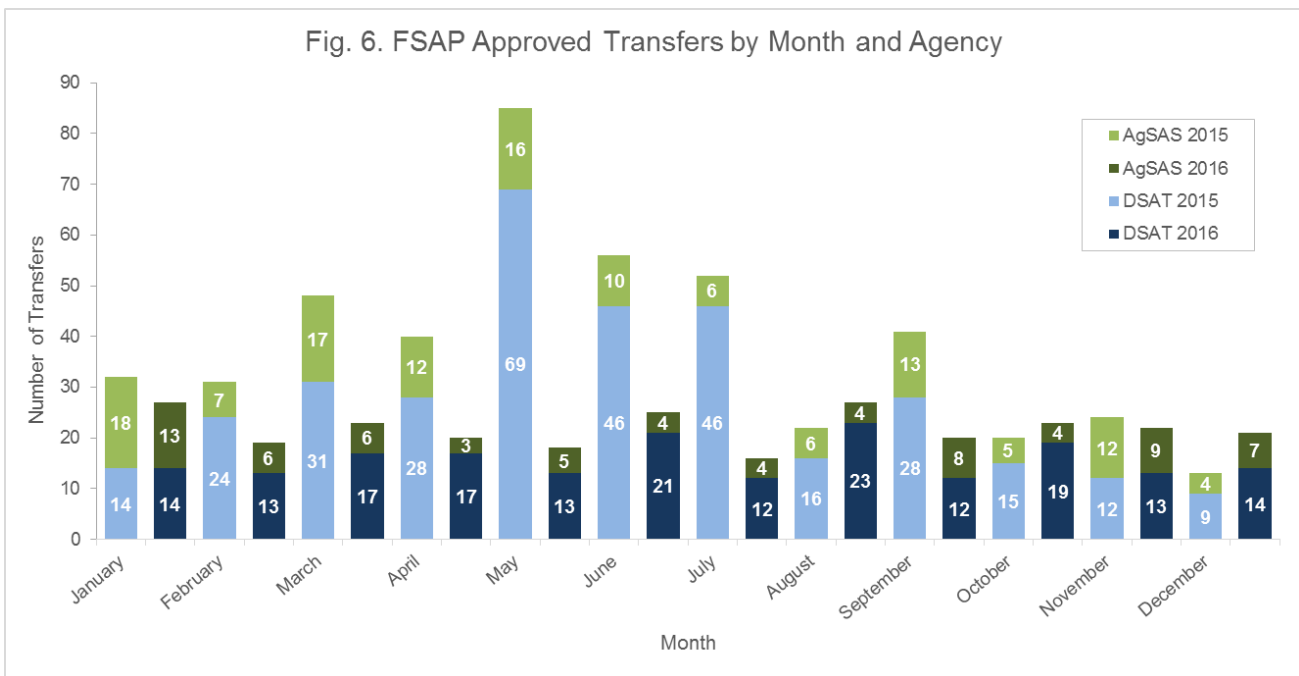
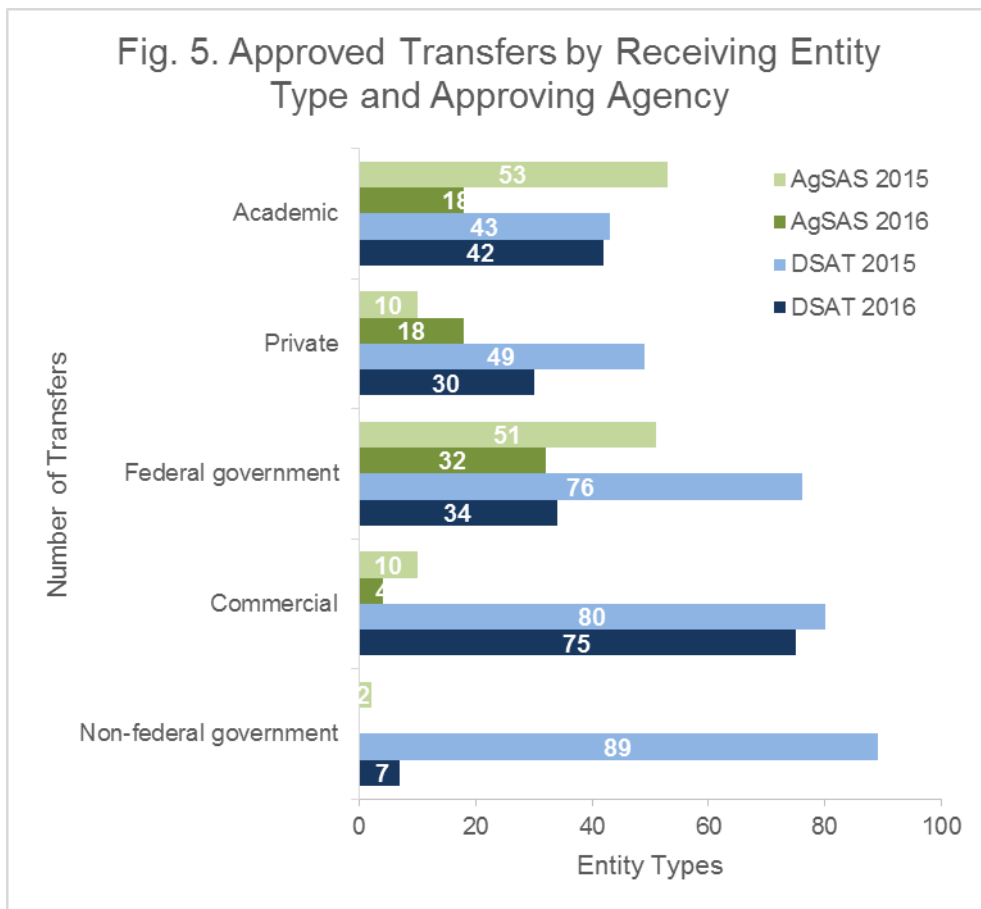


Figure 6 shows the total number of received transfers by approving agency and month in 2016. In contrast to 2015, FSAP did not observe any substantial month-to-month changes during 2016 as the numbers of FSAP-approved transfers per month ranged from 16 to 27 over the course of the year.

## Theft, Loss, and Release of Select Agents and Toxins

The Report of Theft, Loss, or Release (TLR) of Select Agents and Toxins ([APHIS/CDC Form 3](#)), is used by entities to report a theft, loss, or release of BSAT. An entity is required by regulation (7 CFR § 331.19, 9 CFR § 121.19, and 42 CFR § 73.19) to notify AgSAS or DSAT immediately upon the discovery of a theft (unauthorized removal of BSAT), loss (failure to account for BSAT), or release (occupational exposure or release of BSAT outside of primary containment, like a biosafety cabinet) of BSAT. Clinical or diagnostic laboratories and other non-registered entities that possess, use, or transfer BSAT within a specimen presented for diagnosis, verification, or proficiency testing must immediately report this information if there has been a theft, loss, or release of BSAT. Any incident that results in the activation of a post-exposure medical surveillance/prophylaxis protocol should be reported as a release. Examples of a release can include:

- Bites or scratches from infected animals.
- Accidental sticks with needles or other sharps.
- Spills of BSAT materials outside of a biosafety cabinet (BSC).
- Failure or problem with Personal Protective Equipment (PPE) that results in a potential occupational exposure.
- Work outside of BSC with unknown samples later determined to be BSAT.

As in many work places, accidents and incidents also occur in laboratories working with BSAT, though laboratory staff work hard to minimize these events. Laboratory standard operating procedures are in place to ensure worker safety and security of BSAT. Failure to follow standard operating procedures can result in potential releases of BSAT. The risk posed by accidents and incidents is difficult to quantify; out of an abundance of caution, FSAP considers these events as potential exposures.

In 2016, FSAP received 196 APHIS/CDC Form 3 reports of releases and 9 APHIS/CDC Form 3 reports of a loss of BSAT. By comparison, in 2015 FSAP received APHIS/CDC Form 3 reports of 233 releases and 12 losses.

- Of the 196 APHIS/CDC Form 3 reports of releases, 177 reports were determined to represent potential occupational exposure to laboratory workers. The remaining 19 reports involved instances where facility or laboratory personnel were appropriately protected against the released BSAT.

FSAP considers all persons that entered the laboratory space who were not appropriately protected while these samples were being manipulated outside of primary containment as potentially exposed. Of the 177 potential occupational exposure events:

- 78 events occurred at registered entities and 99 occurred at unregistered entities.
  - Of the 99 events reported by unregistered entities, 97 occurred in laboratories performing diagnostic procedures on patient specimens to inform care decisions, one occurred during an operation on a patient later identified as infected with BSAT, and one resulted from a spill of cultures later confirmed to contain BSAT.
  - Of the 78 events reported by registered entities, 7 occurred following bites or scratches from animals infected with BSAT, 10 resulted from failures of equipment used for work with BSAT, 9 occurred following contact with potentially contaminated needles and other sharp objects, 11 resulted from PPE that became compromised, 7 occurred as a result of deviation from proper safety procedures or training, 19 ensued from BSAT spills outside of primary containment, and 15 occurred following manipulation of BSAT outside of primary containment equipment protecting workers from exposure to infectious aerosols.
- 998 laboratory workers (194 at registered entities, 804 at unregistered entities) were provided occupational health services, including medical assessments and monitoring, diagnostic testing, and prophylaxis as necessary. In 2015, 908 laboratory workers (712 at unregistered entities) were provided these services.

- 779 of the 804 exposed laboratorians at unregistered entities worked with the unknown diagnostic samples outside of a BSC prior to their identification as BSAT. In 2015, FSAP identified 671 laboratorians at unregistered entities that were exposed to BSAT outside of a BSC.
- 38 of the 194 laboratorians were exposed to BSAT at registered entities while working on unknown diagnostic samples outside of a BSC. In 2015, 25 of the 196 exposed laboratorians were exposed to the BSAT outside of a BSC.
- In 2015 and 2016 no potential releases resulted in transmission of pathogens outside of the laboratories, illnesses in any of the potentially exposed individuals, or deaths.

The FBI was notified about eight of the nine APHIS/CDC Form 3 reports of losses. The FBI investigated all eight losses, and determined that there was no criminal nexus in any of the cases. The FBI was not notified about one of the nine losses because the entity recovered the select agent.

FSAP received no reports of thefts of BSAT in 2016.

## Emergency Response

FSAP reaches out to assist entities with transferring or securing BSAT that may be affected by adverse weather events that could affect the safety of employees and security of BSAT. There were 14 adverse weather events in 2016, and FSAP contacted a total of 86 affected entities. By comparison, FSAP responded to 13 adverse weather events that affected 121 entities in 2015. Table 9 summarizes FSAP's assistance efforts during weather emergencies in 2016. All affected entities were successfully contacted and none required FSAP assistance. There were no thefts, losses, or releases of BSAT as the result of any weather emergencies in 2016.

**Table 9. FSAP Emergency Response Events, 2016**

2016 Event	# of Entities Contacted
East Coast Tornadoes	12
LA/MS Floods	2
Houston, TX Flooding	5
Southeastern TX Flooding	10
WV Flooding	1
Tropical Storm Darby	2
Hamilton MT Wildfire	1
LA/MS Flooding	3
Hurricane Hermine	8
Hurricane Lester	3
Earthquake near Pawnee, OK	1
IA Flooding	1
Pre/Post Hurricane Matthew	36
Earthquake near Cushing, OK	1
Total	86

## Federal Register Notices, Policy Statements, and Guidance

FSAP publishes policy, regulatory, and guidance updates for changes that effect the regulated community. FSAP issued a total of 19 Federal Register notices, policy statements, and guidance in 2016 (Table 10), compared with five FSAP issuances in 2015. The increase in FSAP issuances in 2016 is due to a concerted effort by FSAP to engage and partner with the regulated community to identify solutions that improve compliance with the regulations. FSAP policies and guidance documents can be found on the FSAP [website](#). Some examples of FSAP issuances are included in Table 10.

**Table 10. FSAP Federal Register Notices, Policy Statements, and Guidance, 2016**

Federal Register Notices	Policy Statements	Guidance
Federal Register/Advance Notice of Proposed Rulemaking regarding the biennial review and republication of the list of <a href="#">HHS</a> and <a href="#">USDA</a> select agents and toxins (January)	Inspection Observation Dispute Process (March)	Select Toxin Guidance Document (June)
<a href="#">Publication of Interim Final Rule – <i>B. cereus</i> Biovar <i>anthracis</i></a> (September)	Revised "Inactivated <i>Bacillus anthracis</i> " policy statement (June)	Guidance on Drills and Exercises (June)
	Requesting Access for Personnel at Multiple Entities (August)	
	Requests for Transfer of Select Agents and Toxins (September)	
	Revised "Inactivated <i>Bacillus anthracis</i> " policy to include <i>B. cereus</i> Biovar <i>anthracis</i> (September)	

## Outreach

FSAP has an active outreach program designed to provide opportunities for the program to interact with members of the regulated community. Table 11 and the bullets below summarize the 2016 FSAP outreach initiatives and events.

- Developed an anonymous feedback survey that is sent to recently inspected entities to gauge FSAP performance during inspections and to identify areas to improve the inspection process.
- Conducted a multi-day Responsible Official Workshop to provide information about maintaining regulatory compliance and build community among those working in this area.
- Conducted a webinar to provide information on changes to the FD-961 Bioterrorism Risk Assessment Form.
- Distributed updates to registered entities regarding changes to FSAP leadership, policies, regulatory interpretation, and workshop information via the SA Gram, an electronic communication used periodically by FSAP to disseminate information to the regulated community.
- Exhibited an informational booth at seven scientific conferences to provide guidance and promote compliance with the SAR.

**Table 11. FSAP Outreach Events, 2016**

<b>Conference</b>	<b>Dates</b>
CDC International Symposium on Biosafety	January 31-February 2, 2016
American Society for Microbiology (ASM) Biodefense and Emerging Diseases Research Meeting	February 8-10, 2016
2016 American Public Health Laboratories Annual Meeting	June 6-9, 2016
2016 ASM Microbe Annual Meeting	June 17-20, 2016
ABSA International Annual Conference	September 30-October 5, 2016
American Association of Animal Laboratory Science	October 31-November 2, 2016
American Public Health Association	October 30-November 2, 2016
<b>Workshop</b>	<b>Date</b>
FSAP Responsible Official Workshop	December 6-8, 2016
<b>Webinar</b>	<b>Date</b>
FSAP Webinar, Changes to FD-961 Bioterrorism Risk Assessment Form	April 19, 2016

## References

[Select Agents and Toxins Regulations](#). 7 CFR Part 331, 9 CFR Part 121, 42 CFR Part 73.

[Biosafety in Microbiological and Biomedical Laboratories](#) (BMBL) 5th Edition. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Institutes of Health, HHS Publication No. (CDC) 21-1112. Revised December 2009.

[NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules](#) (NIH Guidelines). U.S. Department of Health and Human Services, National Institutes of Health. April 2016.

**Transfer of Select Agents and Toxins, 2003-2013.** Division of Select Agents and Toxins, Centers for Disease Control and Prevention. Shelby BD, Cartagena D, McClee V, Gangadharan D, Weyant R. Health Security. August 2015 Vol. 13, No. 4 256-66.

[2015 Annual Report of the Federal Select Agent Program](#). U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and US Department of Agriculture, Animal and Plant Health Inspection Services. June 2016.

Please send requests for additional information to FSAP at [LRSAT@cdc.gov](mailto:LRSAT@cdc.gov) or [AgSAS@aphis.usda.gov](mailto:AgSAS@aphis.usda.gov).