Overview of the Federal Select Agent Program and Import Permit Programs

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&

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Importation of Biologicals Workshop
U.S Customs and Border Protection
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U.S. Federal Biosafety & Biosecurity Oversight

All Workplace Hazards
OSHA General Duty Clause (Regulatory)

Certain Infectious Agents
Transport, Export, Import (DOT, DOC, CDC, APHIS) (Regulatory)

Bloodborne Pathogens
OSHA Standard (Regulatory)

Infectious Agents
NIH/CDC BMBL (Voluntary)

Select Agents
HHS/USDA Select Agent Regulations (Regulatory)

Recombinant DNA
NIH Guidelines (Condition of NIH funding)
FEDERAL SELECT AGENT PROGRAM
Federal Select Agent Program (FSAP)

- FSAP regulates the possession, use, and transfer of biological agents and toxins that have the potential to pose a severe threat to public, animal or plant health, or to animal or plant products

- Managed jointly by:
  - The Division of Select Agents and Toxins (DSAT) at the Centers for Disease Control and Prevention (CDC), part of the U.S. Department of Health and Human Services (HHS)
  - The Agriculture Select Agent Services (AgSAS) at the Animal and Plant Health Inspection Service (APHIS), part of the U.S. Department of Agriculture (USDA)
Overview & History

- 2001 anthrax attacks led to strengthening of program
- Title II of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002
  - Legal authority for the current Federal Select Agent Program
  - Required security measures in addition to biosafety measures
  - Strengthened the regulatory authorities of HHS
  - Granted comparable regulatory authorities to USDA
Title II of The Act: Enhanced Control of Dangerous Biological Select Agents and Toxins

- Establish a list of biological select agents and toxins
  1. Effect of exposure
  2. Degree of contagiousness and method of transmission
  3. Availability of effective pharmacotherapies and immunizations
  4. Other criteria determined to be appropriate by the Secretary

- Consult with other federal departments and agencies, as well as scientific experts representing appropriate professional groups

- Review/republish the list biennially, or revise as often as needed
Types of Select Agents and Toxins

- **HHS-only agents** (HHS has sole authority and responsibility to regulate)
  - Potential to affect public health and safety
  - Botulinum neurotoxins, *Yersinia pestis*, Smallpox virus

- **USDA-only agents** (USDA has sole authority and responsibility to regulate)
  - Potential to affect animal & plant health; animal & plant products
  - Foot-and-mouth disease virus, Rinderpest virus

- **“Overlap” agents**
  - Subject to regulation by both agencies because they have potential to affect both humans and animals (requires interagency coordination)
  - *Bacillus anthracis*, *Brucella abortus*, Rift Valley fever virus
67 agents and toxins on the HHS and USDA list:
- 35 HHS-only
- 21 USDA-only
- 11 Overlap (HHS/USDA)
- 14 Tier 1 agents

https://www.selectagents.gov/SelectAgentsandToxinsList.html
Tier 1 Select Agents and Toxins

- Tier 1 is a subset of the select agents and toxins list that presents the greatest risk of deliberate misuse with the most significant potential for mass casualties or devastating effects to the economy, critical infrastructure, or public confidence.

<table>
<thead>
<tr>
<th>HHS select agents and toxins</th>
<th>USDA select agents</th>
<th>Overlap select agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) <em>Bacillus cereus</em> Biovar <em>anthracis</em></td>
<td>(1) Foot-and-Mouth Disease virus</td>
<td>(1) <em>Bacillus anthracis</em> (excluding Pasteur strain)</td>
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<td>(2) Botulinum neurotoxin</td>
<td>(2) Rinderpest virus</td>
<td>(2) <em>Burkholderia mallei</em></td>
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<tr>
<td>(3) Botulinum neurotoxin producing species of Clostridium</td>
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<td>(3) <em>Burkholderia pseudomallei</em></td>
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<td>(4) Ebola virus</td>
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<td>(5) <em>Francisella tularensis</em></td>
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<td>(6) Marburg virus</td>
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<td>(7) Variola major virus</td>
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<td></td>
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<tr>
<td>(8) Variola minor virus</td>
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<tr>
<td>(9) <em>Yersinia pestis</em></td>
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</table>
Key Regulatory Functions & Activities

- Promulgate the select agent regulations
- Provide oversight of possession, use, and transfer
- Conduct inspections and approve registrations
- Approve individual access to select agents & toxins
- Receive reports of a theft, loss, or release
- Take appropriate enforcement actions
- Serve as a resource on compliance with the regulations
Types of Entities Registered with FSAP, 2017

Total: 263

- Academic: 33%
- Commercial: 18%
- Federal Government: 15%
- Non-Federal Government: 29%
- Private: 6%

Inspection Types

- Compliance
- Maximum containment
- New entity
- New space
- Renewal
- Verification
FSAP Inspection Basics

- **Biosafety**
  - Entity-specific biosafety plan
  - Standards described in *Biosafety in Microbiological and Biomedical Laboratories* (BMBL, 5th edition) or equivalent
  - NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules
  - Notification of release
  - Select agent inactivation

- **Biosecurity**
  - Entity-specific security plan
  - Security risk assessments of individuals
  - Access controls
  - Inventory and accountability
  - Notification of theft or loss
  - Tier 1 agents and toxins, 3 security barriers, and suitability assessment for individuals

  *Training; drills or exercises*
Select Agent Enforcement

- **Voluntary action**
  - Corrective Action Plan (CAP)

- **Administrative actions**
  - Denial of application
  - Revocation or suspension of registration

- **Civil money penalties**
  - Up to $250k for an individual for each violation
  - Up to $500k for an entity for each violation

- **Criminal**
  - Imprisonment for up to 5 years, a fine, or both
The 2017 Annual Report of the Federal Select Agent Program continues to provide insight into the regulatory activities of the Federal Select Agent Program (FSAP). The report includes a look at both the regulatory functions of the program, as well as compliance with the select agent regulations at laboratories across the nation. This annual report is FSAP’s third report of aggregate program data, and reflects the program’s ongoing commitment to transparency and increasing understanding of the program.

- FSAP is managed jointly by the Centers for Disease Control and Prevention’s Division of Select Agents and Toxins and the Animal and Plant Health Inspection Service’s Agriculture Select Agent Services.
- FSAP regulates the possession, use, and transfer of biological select agents and toxins (BSAT) so that important work with potentially dangerous and deadly pathogens is conducted as safely and securely as possible.
- BSAT are materials that have the potential to pose a severe threat to public, animal or plant health, or to animal or plant products.

### Compliance & Enforcement

- **8** total entities participated in a corrective action plan (including **1** entity that newly agreed to participate in 2017).
- **4** total entities had suspended registrations (including **2** entities newly put under suspension in 2017).
- **18** matters were shared with the Federal Bureau of Investigation for potential investigation (no action was needed in **17** of those cases, with one pending).
- **7** entities were referred to the HHS Office of Inspector General or APHIS Investigative and Enforcement Services.

### Theft, Loss, or Release

- **0** thefts reported.
- **9** reports of losses determined to be records management errors.
- **199** incidents reported involving potential occupational exposure of 1,152 laboratory workers.
- **0** potential exposures resulting in illness, death, or transmission.

### Transfer Approvals: 177 DSAT | 79 AgSAS

- **29%** of the transfers were from unregistered entities to registered entities, mostly as a result of identification of BSAT in a diagnostic specimen.

### Key Abbreviations:

- **FSAP**: Federal Select Agent Program
- **DSAT**: Division of Select Agents and Toxins
- **BSAT**: Biological select agents and toxins
- **ABSL**: Animal biosafety level
- **CDC**: Centers for Disease Control and Prevention
- **APHIS**: Animal and Plant Health Inspection Service
- **AgSAS**: Agriculture Select Agent Services

*Tier 1 agents, those that pose the greatest risk through misuse.*

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Program Metrics

Since 2003, there have been:

- **No** reported thefts of a select agent or toxin from a registered entity
- **No** deaths among laboratory workers
- **No** reported cases of illness or death in the general public due to work with these agents in regulated laboratories
Needs for Transformational Change

- Public Health Security and Bioterrorism Preparedness and Response Act of 2002 requirement to maintain database
- GAO’s recommendation to improve coordination and oversight
- National Biodefense Strategy – 2018
- FSAP Strategic Plan developed covering multiple aspects of the program – focus on system as force multiplier making it possible

FSAP Strategic Plan
1. Ensure the recruitment, development, and retention of a knowledgeable and professional FSAP workforce
2. Harmonize FSAP organizational processes and inspections
3. Leverage data-driven, risk-based approaches to guide FSAP operations
4. Engage, increase transparency, and highlight program benefits, with FSAP’s diverse stakeholders
Electronic FSAP (eFSAP) Information System

- Secure, web-based user interface (portal)
- Searchable; will provide immediate, real-time information on who has what select agents, how they are being used in the work, and where they are located
- Increased efficiency; FSAP can be more timely and effective
- FSAP and regulated entities will both use the set of data
- Reduced paper
- New method of releasing inspection findings can help entities work towards resolution in days vs. weeks or months
Burden Reduction and Customer Satisfaction

- Many aspects of entity registration maintenance have been revamped to be self-service
  - Reduces administrative burden for both program and entity
  - Significantly speeds up processing

- Increased ease of validating and submitting information

- Entities have immediate visibility of where their submissions are in life cycle

- Direct interaction between SMEs and entity representatives

- Informal and anecdotal commendations for the enhancements
  - Looking forward to formalized surveys next spring
eFSAP Information System: Accelerated Processing Times

Processing times for adding individuals, amendment & renewal processing
For More Information

www.selectagents.gov

CDC: lrsat@cdc.gov or 404-718-2000

APHIS: AgSAS@usda.gov or 301-851-3300 option 3 (voice only)
IMPORT PERMIT PROGRAMS
Both APHIS and CDC have import permitting units, for non-select biological materials that could cause or introduce agricultural or human disease (respectively).

These programs help ensure that the importation (CDC + APHIS) and/or interstate transport (APHIS) of these agents is monitored and that facilities receiving permits have appropriate biosafety measures in place to work with the permitted agents.
CDC Import Permit Program (IPP)

Thomas Cremer, PhD & Glen DeGruy, MS.
IPP: Background

- Regulates the importation of infectious biological materials that could cause disease in humans in order to prevent their introduction and spread into the U.S.

- The regulations require that anyone wishing to import infectious biological agents, infectious substances, or vectors associated with communicable disease in humans must first obtain a permit issued by CDC
Ensures that the importation of these agents is monitored and that facilities receiving permits have appropriate biosafety measures in place to work with the imported agents.

More than 2,000 import permits issued annually.

Most issued to laboratory facilities at government agencies and universities, or to private and commercial laboratories conducting research studies or diagnostic activities.

No fee.

![Import Permits Issued by Year](chart)
Materials Requiring Permits

- Infectious biological agents capable of causing illness in humans
- Materials known or reasonably expected to contain an infectious biological agent
- Vectors of human disease (e.g., insects, bats)
### Most commonly imported agents (2017):

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<thead>
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<tbody>
<tr>
<td><strong>1</strong></td>
<td>Human Immunodeficiency Virus</td>
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<tr>
<td><strong>2</strong></td>
<td><em>Escherichia coli</em></td>
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<tr>
<td><strong>3</strong></td>
<td>Zika virus</td>
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<tr>
<td><strong>4</strong></td>
<td>Hepatitis c virus</td>
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<tr>
<td><strong>5</strong></td>
<td>Hepatitis b virus</td>
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<tr>
<td><strong>6</strong></td>
<td>Dengue virus</td>
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<tr>
<td><strong>7</strong></td>
<td>Cytomegalovirus</td>
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<tr>
<td><strong>8</strong></td>
<td><em>Streptococcus</em> species</td>
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<tr>
<td><strong>9</strong></td>
<td><em>Salmonella</em> species</td>
</tr>
<tr>
<td><strong>10</strong></td>
<td><em>Staphylococcus</em> species</td>
</tr>
</tbody>
</table>
Key Regulatory Functions & Activities of IPP

- Issues permits
- Conducts inspections to ensure appropriate biosafety measures are in place
- Provides outreach and training
- Collaborates with federal partners

CDC Import Permit Inspections, 2013-2017
eIPP Information System

- Two-way portal for submitting and sharing information; accessible by both the program and those seeking import permits
- System is electronic-based, user-friendly and allows for real-time updates on the status of pending applications
- Use of this system is mandatory for anyone applying for a CDC import permit
eIPP: Benefits

- Faster processing time for permits
- Provides a centralized location where applicants can get status updates
- Saves user time when applying for future permits
- Provides applicants with a historical record of permits
- Improved communication between applicants and IPP
For More Information

- **CDC Import Permit Program**
  - Phone: (404) 718-2077
  - Fax: (404) 718-2093
  - Email: importpermit@cdc.gov

[https://www.cdc.gov/cpr/ipp/index.htm](https://www.cdc.gov/cpr/ipp/index.htm)
USDA Plant Protection and Quarantine
Select Agent Permitting
Regulation

- All plant pathogen permits are under the Plant Protection Act
  - Regulation 7 CFR § 330.200

“No person shall knowingly move any plant pest into or through the United States from any place outside thereof, or interstate, or knowingly accept delivery of any plant pest...unless such movement is authorized under permit under this part and is made in accordance with the conditions therein and the provisions in this part.”
ePermits

- All permits are processed through the ePermits system
- Applicants must be eAuthenticated to submit a permit application
- Applicants applying for select agents must go through the select agent pathway
  - All applications can only be seen by AgSAS
  - Applicants must be registered with the FSAP
    - Exclusions from SA conditions for applicants applying for Ralstonia solanacearum non Race 3 Biovar 2
- All permitees must abide by the conditions in the permit and all facilities will be inspected
Movement of Select Agents

Select Agent Movement Types

- Importation
- Interstate Movement
- Intrastate Movement
- Continued Curation
Hand Carry

- Permit must have “hand-carry” listed as an option for transport
- Importation- applicant needs to request a letter from AgSAS to show Customs Officer when entering the country along with the permit
  - The package can be sent to CPHST 580 in Beltsville if Customs deems it needs to be assessed
APHIS Organisms and Vectors Import Permitting
9 CFR Part 122

“No organisms or vectors shall be imported into the United States or transported from one State or Territory or the District of Columbia to another State or Territory or the District of Columbia without a permit”
Materials Requiring Permits: ORGANISMS

- Livestock and poultry pathogens
- DNA, RNA, killed pathogens
- Any organism exposed to livestock or poultry materials
Materials Requiring Permits: VECTORS

- Arthropods, parasites
- Animal samples
- Animal products
- Vectors, plasmids with pathogen genes
Organisms and Vectors Permitting

Last modified: Apr 2, 2019

The Veterinary Services, Organisms and Vectors (OV) Permitting Unit regulates the importation into the United States, and interstate transportation, of organisms and vectors of pathogenic diseases of livestock and poultry.

The Code of Federal Regulations, 9 CFR, §122.2, mandates that no organism or vectors shall be imported into the United States or transported from one State or Territory or the District of Columbia to another State or Territory or the District of Columbia without a permit.

USDA Issues Guideline 1125 – Effective April 15, 2019

Vet Services will implement changes to permitting requirements based on Guideline 1125, effective April 15, 2019. The guideline describes allowances for non-regulated international movement of certain materials such as non-infectious materials and materials that have not been exposed to infectious agents. To view Guideline 1125 in its entirety, please click here.

Types of Permits

How to Apply for a VS Form 18-3 Permit

Additional Resources

Additional Information

- Animal and Animal Product Import Information
- Agriculture Select Agent Services
- Organisms and Vectors Guidelines
- On Hold Shipment
- Veterinary Biologics
- Plant Pest and Disease Programs
- Biotechnology Regulatory Services
- Center for Disease Control and Prevention’s (CDC) Import Permit Program (IPP) (Opens in new window)
- U.S. Fish and Wildlife Services permits (Opens in new window)
Organisms and Vectors Guidance

- Do I Need an OV Permit?
- VS-Regulated Livestock and Poultry Pathogens
- Excluded and/or Killed Select Agent Pathogens that May Need an OV Permit
- Guideline 1125: Conditions Under Which Veterinary Services (VS) Does Not Require an Interstate Transportation Permit for Organisms and Vectors
- Frequently Asked Questions: For Importation and Transportation Of Organisms and Vectors (OV)

Additional Information
- Animal and Animal Product Import Information
- Agriculture Select Agent Services
- Organisms and Vectors Permitting
- On Hold Shipment
- Veterinary Biologics
- Plant Pest and Disease Services
- Biotechnology Regulatory Services
- Center for Disease Control and Prevention’s (CDC) Import Permit Program (IPP) []
- U.S. Fish and Wildlife Service permits []
VS-regulated livestock and poultry pathogens (partial list, Revised 3/21/2019)

Absidia corymbifera
Acremonium strictum
Acinetobacter spp. **
Actinobacillus pleuropneumoniae
Actinomyces bovis
Aedes mosquito
Aedes mosquito eggs
Aeromonas hydrophila
Aeromonas spp. **
African horse sickness (only the excluded select agent*)
African swine fever (only the excluded select agent*)
Akabane virus
Alcaligenes faecalis
Amblyomma spp. - tick
Amidostomum anseri
Amycolaptosis spp. **
Anaplasma centrale
Anaplasma marginale
Anaplasma phagocytophilum
Anopheles mosquito eggs
Anopheles mosquitos
Guidelines: Animal Products That Do Not Require An Import Permit

These materials **do not** require a USDA import permit, but will be reviewed at the port of entry.

- Guideline 1100: Human And Veterinary Pharmaceuticals and Vaccines
- Guideline 1101: Non-Human Primate Material (excluding cell cultures)
- Guideline 1102: Feline and Canine Material
- Guideline 1103: Live Laboratory Mammals and Their Material (for research purposes)
- Guideline 1104: Amphibians, Fish, Reptiles, Shellfish and Aquatic Species (includes venom)
- Guideline 1105: Chemically Synthesized Materials
- Guideline 1107: Importation of Lactose and Lactose Derivatives
- Guideline 1110: Microbially Produced Materials
- Guideline 1114: Recombinant Microbes and Their Products
- Guideline 1116: Non-Pathogenic Microorganisms (and their extracts)
- Guideline 1119: Pet Chews and Treats Made of Antlers or Rawhide
- Guideline 1120: Cell Cultures/Lines, Recombinant Cell Cultures/Lines, and Their Products (for in vitro use)
- Guideline 1121: Self-Contained Test Kits Containing Animal-Derived Ingredients
- Guideline 1122: Vitamins and Minerals
- Guideline 1123: Histopathological Fixed Slides
For More Information

- APHIS Organisms and Vector Permitting
  - Email: OV@usda.gov
  - Phone: 301-851-3300, option 3
  - Staff Officers: Deb Dufficy, Troy Bigelow
Discussion