



Overview of Select Agent Regulations

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Objectives

Participants will be able to identify the following:

- Select Agent regulations and requirements
- Select Agents/Proposed changes
- Exclusions
- Exemptions
- Forms/Requirements

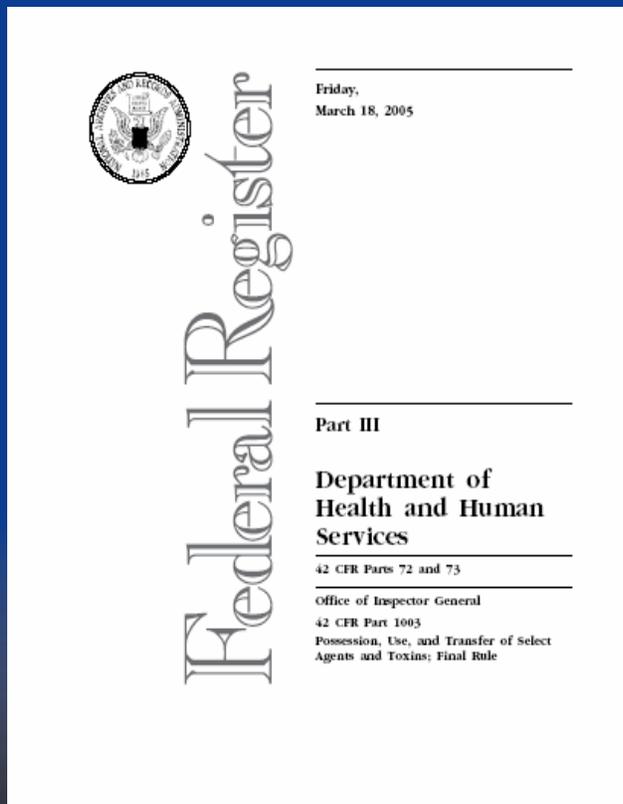


Select Agent Regulations and Requirements

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Final Rules: Possession, Use, and Transfer of Select Agents and Toxins



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

- Publication date: March 18, 2005
- Effective date: April 18, 2005
- Implemented the provisions of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (signed June 12, 2002)



Entity Requirements

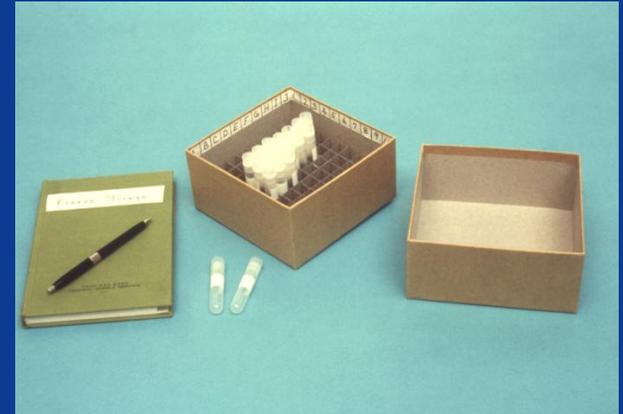
- Register for each select agent or toxin it possesses, uses, or transfers
- Designate a Responsible Official (RO)
- Receive government approval of entity (owners), RO, & individuals who need access to select agents
 - ◆ Based on DOJ check of electronic databases (“Security Risk Assessment” = SRA)
- Allow for inspections by APHIS &/or CDC



Entity Requirements



- Maintain records (3 years):
 - ◆ Inventories
 - ★ Accurate, current
 - ★ All elements under 42 CFR 73.17(a)(1), select agents and 73.17(a)(2), toxins
 - ◆ Access to areas where agents are used or stored
 - ◆ Transfers
 - ◆ Training
 - ◆ All records pertaining to select agents and toxins





Entity Requirements

- Ensure the accuracy of records and databases
- Develop safety, security, and incident response plans
- Conduct drills or exercises at least annually to test and evaluate the effectiveness of these plans
- Conduct safety and security training
 - ◆ Include risks/hazards
 - ◆ SRA-approved individuals and visitors
 - ◆ Tailored to needs of individual and work performed
- Immediate notification of theft, loss, or release



Entity Requirements

- Document, at least annually
 - ◆ BSL3/ABSL3, or BSL4/ABSL4, verification of the facility design and operational parameters, for respective registered laboratories

 - ◆ Biosafety cabinet certification



Entity Requirements

- Request prior approval from CDC/APHIS to perform restricted experiments involving recombinant DNA work that:
 - ◆ Introduces antibiotic-resistant genes into select agents
 - ◆ Produces select toxins lethal for vertebrates at an $LD_{50} < 100$ ng/kg body weight
- Requests reviewed by an Intragovernmental Select Agent and Toxin Technical Advisory Committee



42 CFR 73.12 Biosafety



Develop and implement a safety plan:

- For BSL 2-4 select agents:
 - ◆ Biosafety in Microbiological and Biomedical Laboratories, Fifth edition, February 2007.
- For toxins:
 - ◆ 29 CFR 1910.1450 Occupational Exposure to Hazardous Chemicals in Laboratories.
 - ◆ 29 CFR 1910.1200 Hazard Communication (for laboratories distributing toxins).
 - ◆ Appendix I: Guidelines for Work with Toxins of Biological Origin.
- For recombinant select agents:
 - ◆ Guidelines for research involving recombinant DNA molecules (NIH Guidelines), April 2002.



42 CFR 73.11 Security



■ Access

- ◆ “An individual will be deemed to have access at any point in time if the individual has possession of a select agent or toxin (e.g., ability to carry, use, or manipulate) or the ability to gain possession of a select agent or toxin.”



■ Restricting access

- ◆ Physical barriers
 - ★ Locks on doors and storage containers
 - ★ Card or key pads
- ◆ Escorted and continually monitored by an authorized and approved person





42 CFR 73.11 Security

- **The security plan must:**
 - ◆ Be sufficient to safeguard the select agent or toxin against unauthorized access, theft, loss, or release
 - ◆ Be based upon a site-specific risk assessment
 - ◆ Include all elements of 42 CFR 73.11

- See Guidance Document:
www.selectagents.gov/securitydoc.htm



42 CFR 73.14 Incident Response

The incident response plan must:

- Be coordinated with entity-wide plans, kept in the workplace, and available to employees
- Include all elements of 42 CFR 73.14
- Include planning and coordination with local emergency responders



Requirements to be Performed at Least Annually

Documentation of:

- Drills or exercises
- Review plans (biosafety, security, and incident response)
- Safety and security training
- Inspections - all parts, 42 CFR 73
- Verification of facility design and operational parameters (BSL3/BSL4)
- BSC certification



Select Agents

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Types of Select Agents and Toxins



HHS-only Agents (HHS has sole authority and responsibility to regulate)

- Select agents and toxins that have the potential to pose a severe threat to public health and safety

USDA-only Agents (USDA has sole authority and responsibility to regulate)

- Select agents and toxins that have the potential to pose a severe threat to animal or plant health, or to animal or plant products

Overlap Agents

- Select agents and toxins subject to regulation by both agencies



Select Agents and Toxins

Complete list:

- HHS select agents and toxins, 42 CFR 73.3
- Overlap select agents and toxins, 42 CFR 73.4
- Section 3, APHIS/CDC Form 1 (see handout)



HHS, USDA, & Overlap Select Agents And Toxins



(as of 10/20/05)

	<u>HHS</u>	<u>Overlap</u>	<u>USDA</u>
Viruses	10	5	19
Bacteria	3	9	3
Fungi	1	1	0
Toxins	7	5	0
Plant Path	0	0	8
Prion	<u>0</u>	<u>0</u>	<u>1</u>
	21	20	31



Changes to Select Agent and Toxin List



(Proposed, as of 8/28/07)

- HHS/CDC published a notice of proposed rulemaking in the *Federal Register*, 8/28/07 (see www.selectagents.gov)
- In response to USDA's proposal to no longer regulate 10 select agents and toxins currently listed as "overlap" agents and toxins, the CDC is proposing to regulate these as HHS-only agents and toxins.
- Comments on proposed change due by 10/29/07 (SAPcomments@cdc.gov)



Proposed Changes to Select Agent List

(Proposed on 8/28/07)

Overlap to HHS List:

- Botulinum neurotoxin producing species of *Clostridium*
- *Coxiella burnetii*
- *Francisella tularensis*
- Eastern equine encephalitis virus
- *Coccidioides immitidis* (entry to be revised as *Coccidioides posadasii/Coccidioides immitis*)



Proposed Changes to Select Agent List



(Proposed on 8/28/07)

Overlap to HHS List:

- Botulinum neurotoxins
- T-2 toxin
- Shigatoxin
- Staphylococcal enterotoxin
- *Clostridium perfringens* epsilon toxin



Genetic Elements, Recombinant Nucleic Acids, and Recombinant Organisms



- Nucleic acids that can produce **infectious forms** of any of the regulated select agent viruses, e.g. the positive stranded RNA viruses.

- Recombinant nucleic acids that encode for the functional form(s) of the regulated toxins, if the nucleic acids
 - ◆ Can be expressed *in vivo* or *in vitro*; or
 - ◆ Are in a vector or recombinant host genome and can be expressed *in vivo* or *in vitro*.

- Regulated select agents and toxins that have been genetically modified.



Exclusions

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Exclusions

- Naturally occurring select agents and toxins:
 - ◆ Excluded – if they have not been intentionally introduced, cultivated, collected, or otherwise extracted from their natural source
 - ★ Non-human primates that are naturally infected with Herpes B virus;
 - ★ Castor beans containing ricin.
 - ◆ Not excluded – if they have been intentionally introduced, cultivated, collected, or otherwise extracted from their natural source
 - ★ Tissues from non-human primates infected with Herpes B;
 - ★ Ricin extracted from the castor bean



Exclusions

- Non-viable select agents or non-functional toxins
- Toxins under the control of a principal investigator, treating physician or veterinarian, or commercial manufacturer or distributor are excluded, if:
 - ◆ Specific quantities of toxins if the aggregate amount under the control of a principal investigator, treating physician or veterinarian, or commercial manufacturer or distributor does not exceed the amount specified



Exclusions

- Attenuated strains approved by CDC or APHIS
 - ◆ CDC: not a threat to human health and safety
 - ◆ APHIS: not a threat to animal or plants, or animal or plant products
- Submit request in writing with supporting documentation
- An exclusion is effective upon notification to the applicant
 - ◆ Is listed on the Web site at www.selectagents.gov
 - ◆ Published periodically in the notice section of the Federal Register
- No longer excluded if subjected to manipulations that restore or enhance virulence



Federal Law Enforcement Exclusion

- Select agent or toxin seized by a Federal law enforcement agency provided that:
 - ◆ Report within 24 hours for certain agents
 - ◆ Report the seizure of known select agents or toxins (Report of Identification Form) within 7 calendar days
 - ◆ Secures and reports theft, loss, or release
 - ◆ As soon as practicable transfer to a registered entity (Request to Transfer Form) or destroy and report on the Report of Identification Form



Exemptions

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Exemptions Clinical/Diagnostic

Clinical or diagnostic laboratories and other entities that possess, use, or transfer a select agent or toxin contained in a specimen presented for diagnosis or verification, or proficiency testing, will be exempt from the requirements provided that certain conditions are met.



Qualifying for Clinical/Diagnostic Exemptions



Select agent or toxin must be:

- Within 7 calendar days of identification (diagnosis/verification), or within 90 calendar days of receipt (proficiency testing):
 - ◆ Transferred (according to 42 CFR 73.16)
 - ◆ Destroyed
 - ◆ Retained (if the entity is registered for the select agent or toxin)
- Secured against theft, loss, or release
- Identification must be reported to:
 - ◆ CDC or APHIS and
 - ◆ Other appropriate authorities as required by Federal, State, or local law.



Reporting Requirements



- Identification of certain select agents requires **immediate** notification to APHIS or CDC via facsimile, e-mail, or telephone
- For all select agents or toxins, Report of Identification (APHIS/CDC Form 4) must be submitted within 7 calendar days of identification (diagnosis/verification) or within 90 calendar days of receipt (proficiency testing).
- Less stringent reporting may be allowed during extraordinary circumstances, such as a widespread outbreak.



APHIS/CDC Forms

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APHIS / CDC Forms



APHIS/CDC Form #	Title of Form
1	Application for Laboratory Registration for Possession, Use, and Transfer of Select Agents and Toxins
2	Report of Transfer of Select Agents and Toxins
3	Report of Theft, Loss, or Release of Select Agents and Toxins
4	Report of Identification of a Select Agent or Toxin in a Clinical or Diagnostic Laboratory
5	Request for Exemption of Select Agents and Toxins for Public Health or Agricultural Emergency or Investigational/ Experimental Product



APHIS/CDC Form 2 Request to Transfer



- Prior authorization
 - **Authorization number valid for only 30 days after issuance**
 - Recipient must submit Request to Transfer within 2 business days of receipt
 - Immediate notification to APHIS or CDC
 - ◆ Not received within 48 hours of expected delivery
 - ◆ Release has occurred
- [See 42 CFR 73.16]

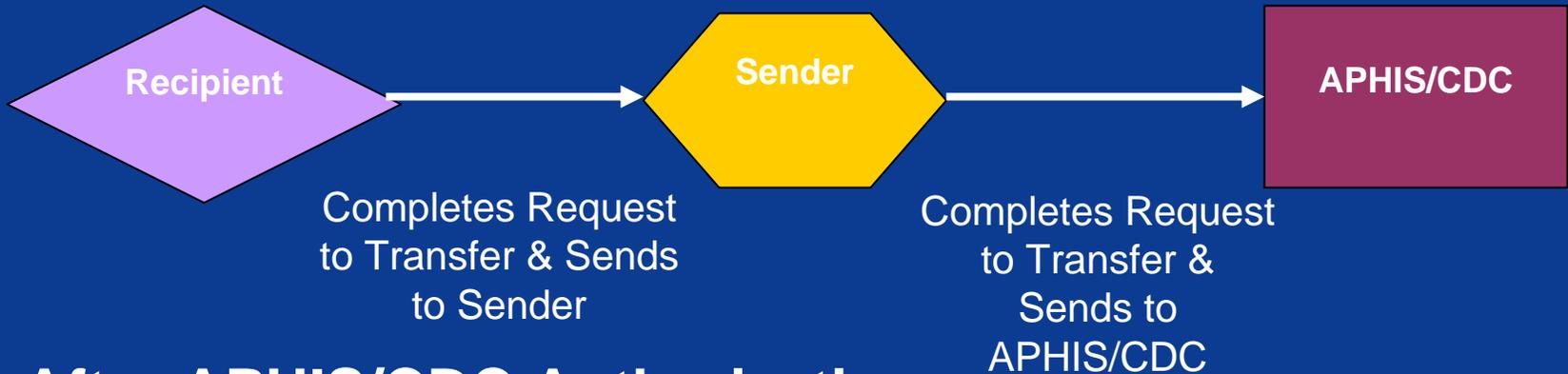
	REQUEST TO TRANSFER SELECT AGENTS AND TOXINS (APHIS/CDC FORM 2)	FORM APPROVED CMB NO. 0575-0213 CMB NO. 0320-0276 EXP DATE 12/31/2008
Read all instructions carefully before completing the report. Answer all items completely and type or print in ink. This report must be signed and submitted to either APHIS or CDC.		
Animal and Plant Health Inspection Service Agricultural Select Agent Program 4700 River Road Unit 2, Mallistop 22, Cubicle 1A07 Riverdale, MD 20737 FAX: 301-734-3652	Centers for Disease Control and Prevention Division of Select Agents and Toxins 1600 Clifton Road NE, Mallistop E-79 Atlanta, GA 30333 FAX: 404-498-2265	
FOR APHIS/CDC USE ONLY		
APHIS/CDC AUTHORIZATION NUMBER: _____		
DATE: _____	INI: _____	EXP DATE: _____
SECTION A - RECIPIENT (REQUESTOR) INFORMATION		
1. Entity name:	2. Entity registration number:	3. a. APHIS Permit # b. US PHS#:
4. Recipient name (authorized personnel) First: MI: Last:	5. Date:	6. Phone: 7. FAX:
Signature:		
8. Principal investigator name (if different from line above) First: MI: Last:	9. Date:	10. Phone: 11. FAX:
Signature:		
12. Responsible Official name First: MI: Last:	13. Date:	14. Phone: 15. FAX:
Signature:		
SECTION B - SENDER (TRANSFEROR) INFORMATION		
16. Entity name:	17. <input type="checkbox"/> Entity registration number: <input type="checkbox"/> Clinical/diagnostic laboratory <input type="checkbox"/> Other:	
18. Sender name First: MI: Last:	19. Date:	20. Phone: 21. FAX:
Signature:		
22. Principal investigator name (if different from line above) First: MI: Last:	23. Date:	24. Phone: 25. FAX:
Signature:		
26. Responsible Official name First: MI: Last:	27. Date:	28. Phone: 29. FAX:
Signature:		



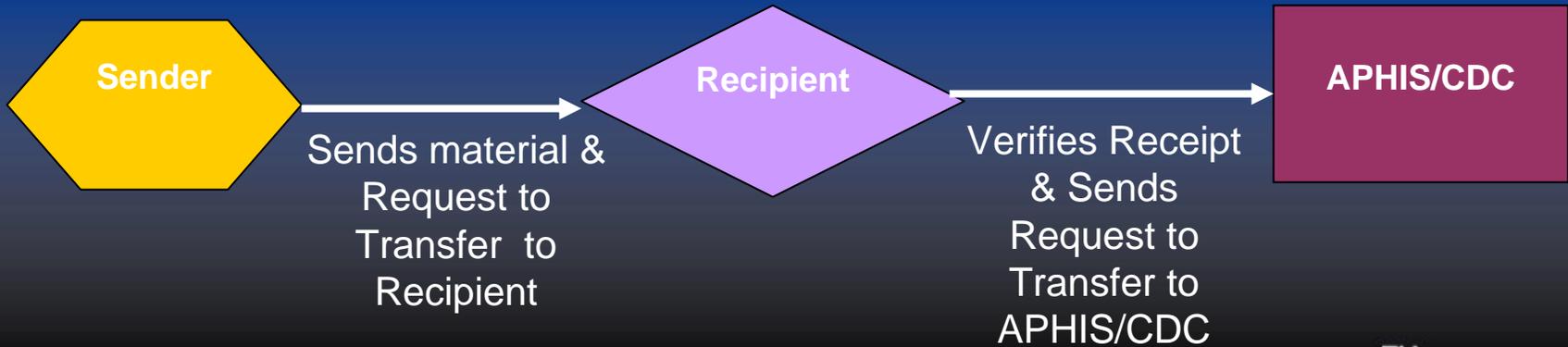
Transfer Process



Prior to Transfer:



After APHIS/CDC Authorization:





APHIS/CDC Form 2 Request to Transfer



- Form 2 Not required:
 - ◆ Transfer of toxins below excluded limits
 - ◆ Transfer of excluded attenuated strains
 - ◆ Transfer of select agents or toxins within a registered entity (intrafacility)
 - ◆ Transfer of select agents or toxins for proficiency testing
 - ◆ Transfer of diagnostic/clinical specimen **before** identified as select agent
 - ◆ Transfer of select agent identified from clinical/diagnostic specimen for antibiotic susceptibility **provided** the request is directly related to diagnosis and verification.



APHIS/CDC Form 3 Report of Theft, Loss, or Release



- Immediate notification of theft or loss:
 - ◆ CDC or APHIS
 - ◆ Appropriate Federal, State, or local law enforcement agencies

USDA **REPORT OF THEFT, LOSS, OR RELEASE OF SELECT AGENTS AND TOXINS (APHIS/CDC FORM 3)** FORM APPROVED OMB NO. 0578-0213 OMB NO. 9205-0216 EXP. DATE 12/31/2008

Read all instructions carefully before completing the report. Answer all items completely and type or print in ink. The report must be signed and submitted to either APHIS or CDC.

Animal and Plant Health Inspection Service
Agricultural Select Agent Program
4700 River Road Unit 2, Mailstop 22, Cubicle 1A07
Riverdale, MD 20737
FAX: 301-734-3552

Centers for Disease Control and Prevention
Division of Select Agents and Toxins
1600 Clifton Road NE, Mailstop E-79
Atlanta, GA 30333
FAX: 404-498-2265

SECTION 1 - TO BE COMPLETED BY ALL ENTITIES

1. Entity name: _____ 2. Entity registration number (if applicable): _____

3. Entity address (NOT a post office address): _____ 4. City: _____ 5. State: _____ 6. Zip Code: _____

7. Responsible Official (RO) or facility director: _____ 8. Telephone: _____ 9. FAX: _____ 10. E-mail: _____
First: _____ Last: _____

11. RO or facility director address (NOT a post office address): _____ 12. City: _____ 13. State: _____ 14. Zip Code: _____

15. Type of incident: Theft Loss Release APHIS CDC
16. Immediate notification provided to: APHIS CDC
17. Date of immediate notification: _____ 18. Type of immediate notification: E-mail Fax Telephone

19. An internal review of laboratory procedures and policies has been initiated to prevent recurrences of loss of select agents and toxins at this entity:
 No Yes (If yes, please provide additional details in an attachment).

SECTION 2 - TO BE COMPLETED BY ALL ENTITIES

LIST OF SELECT AGENTS AND TOXINS LOST, STOLEN OR RELEASED (attach additional sheets if necessary)

20. Select agents and/or toxins:	21. Characterization of agent:	22. Number of vials:	23. Form (powder/liquid/sterile):	24. Vol or wt per vial (e.g., ml, mg, ng):	25. Total quantity:	26. Concentration/vial (e.g., 10 ⁶ pfu/ml):
A						
B						
C						
D						

27. Date and time of incident: _____ 28. Date of last inventory: _____ 29. Name of principal investigator for laboratory with select agents and toxins:
First: _____ Last: _____

30. Location of incident (building and room #): _____ 31. Location of incident (within room (e.g., freezer, incubator)): _____ 32. Biosafety level of laboratory where incident occurred: _____

33. Name and telephone number of agencies or local authorities notified: _____ 34. Symbols or markings on vials (if any): _____ 35. Agent was recovered (theft/loss):
 No Yes

36. Provide a summary of actions taken:
 Called ambulance Called fire department Closed laboratory doors Closed building Consulted MSDS or chemical database
 Called police department (case #) _____ Other (specify): _____

37. Provide a detailed summary of events (attach additional sheets if necessary):

- Immediate notification of release (occupational exposure or release outside primary barriers of biocontainment):
 - ◆ CDC or APHIS

- Submission of form within 7 calendar days

[See 42 CFR 73.19]



For More Information

**APHIS/CDC Select Agent Program web
site: <http://www.selectagents.gov>**

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