## Update: Regulation of Select Agents and Toxins in the U.S.



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## **Evolution of Select Agent and Toxin Regulations**



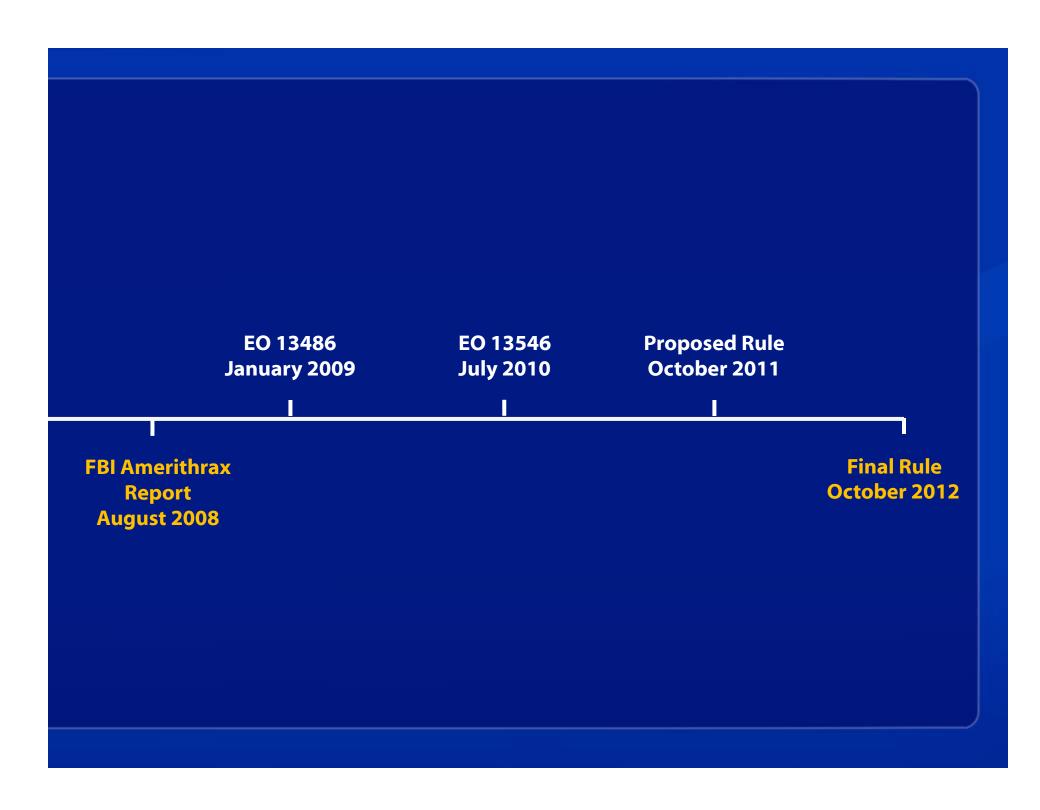
Patriot Act 2001

Bioterrorism Act 2002

Select Agent Final Rule March 2005

Amerithrax Attacks Oct. 2001

BSAT Congressional Hearing Oct. 2007



### October 2012 HHS Select Agents and Toxins Final Rule

- Tiered/Reduced Select Agent List
- Updated Responsible Official requirements
- Specific physical and cyber security requirements for Tier 1 Biological Select Agents and Toxins (BSAT)
- Personnel Suitability Programs for Tier 1 BSAT
- Occupational Health Programs for Tier 1 BSAT
- Broader Definition of Restricted Experiments
- Updated Transfer Requirements



Part III

Department of Health and Human Services

42 CFR Part 73
Possession, Use, and Transfer of Select Agents and Toxins; Biennial Review: Final Rule

### **Effective Dates**

Effective Date	Section
	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 13, 16, 17, 18, 19, 20, and 21
April 3, 2013	11, 12, 14, and 15

## Additions & Removals HHS Select Agent List

#### Additions

- > SARS-associated coronavirus (SARS-CoV)
- > Lujo virus
- > Chapare virus

#### Removals

- Cercopithecine Herpesvirus 1 (Herpes B virus)
- > Clostridium perfringens epsilon toxin
- > Coccidioides posadasii/Coccidioides immitis
- > Eastern Equine Encephalitis virus (South American type only)
- > Flexal virus
- West African clade of Monkeypox viruses
- > Rickettsia rickettsii

### Removals HHS & Overlap Select Agent List

#### Removals from HHS List

- Conotoxins, except short, paralytic alpha conotoxins containing the following nucleic acid sequence
- > Shigatoxins
- Shiga-like ribosome inactivating proteins
- Staphylococcal Enterotoxins, except A, B, C, D, and E subtypes
- Tick-borne encephalitis complex viruses (Central European subtype)

#### Removals from Overlap List

 Venezuelan Equine Encephalitis virus (subtypes 1D and 1E). All other subtypes to remain regulated.

#### **Tier 1 Select Agents and Toxins**

- Ebola and Marburg viruses
- Variola minor and Variola major viruses
- Francisella tularensis
- Yersinia pestis
- Bacillus anthracis\*\*
- Burkholderia mallei and B. pseudomallei
- Botulinum neurotoxin and neurotoxin-producing strains of Clostridium botulinum
- Foot-and-Mouth Disease virus\*
- Rinderpest virus\*

\*USDA-regulated

\*\*Pasteur strain exempt

## Specific security requirements for Tier 1 Select Agent Possessors

#### Suitability assessments

- > Pre-access suitability assessments
- > On-going assessment of the suitability of personnel

#### Physical security standards: access control

- Minimum of three security barriers to reach space that contains Tier 1 BSAT
- Intrusion Detection System

#### **Occupational Health Programs for Tier 1 BSAT**

The biosafety plan must include an occupational health program for individuals with access to Tier 1 select agents and toxins, and those individuals must be enrolled in the occupational health program.

#### **Broader definition of Restricted Experiments**

(a) An individual or entity may not conduct or <u>possess products</u> resulting from a restricted experiment with a select agent or toxin unless approved by and conducted in accordance with any conditions prescribed by the HHS Secretary

(b)(1) Experiments that involve the deliberate transfer of, <u>or selection</u> for, a drug 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.

(b)(2) Experiments involving the deliberate formation of <u>synthetic</u> or recombinant DNA containing genes for the biosynthesis of select toxins lethal for vertebrates at an LD[50] < 100 ng/kg body weight.

# **EXCLUSIONS**

## **Exclusion, Naturally Occurring Select Agents and Toxin**

- Select agent or toxin in its naturally occurring environment is excluded provided that it has not been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source.
  - Non-human primates that are naturally infected with Herpes B virus;
  - Castor beans containing ricin.
- If the select agent or toxin has been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source, then it is no longer excluded.
  - 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.

#### **Exclusion of an Attenuated Strain**

- An attenuated strain of a select agent or an inactive form of a select toxin may be excluded from the requirements of this part based upon a determination by the HHS Secretary or Administrator that the attenuated strain or inactivated toxin does not pose a severe threat to public health and safety, to animal health or to animal products
- To apply, submit a request in writing to the Federal Select Agent Program
  - Must provide documentation establishing that the attenuated strain is eligible for exclusion
- The attenuated strain exclusion is effective upon notification to the applicant
- Listed on the Federal Select Agent Program website at: <a href="http://www.selectagents.gov/Select%20Agents%20and%20Toxins">http://www.selectagents.gov/Select%20Agents%20and%20Toxins</a> %20Exclusions.html
- 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 Tier 1 BSAT
  - 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**

## Exemptions for Diagnostic Laboratories (42 CFR § 73.5)

- General Diagnostic Exemption (42 CFR 73.5(a))
- Proficiency Testing (42 CFR 73.5 (b))
- Possession of products licensed or cleared as an investigational drug by the FDA (42 CFR 73.5 (c)(d))
- Public health emergency (42 CFR 73.5 (e))

## **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.

#### **Impact on Laboratory Response Network**

QA/QC strains	Tier 1	Select agent status
Bacillus anthracis Pasteur	No	regulated
Bacillus anthracis Sterne	No	excluded
Brucella suis 1330 positive control strain	No	regulated
Brucella melitensis 16 M strain	No	regulated
Francisella tularensis LVS	No	excluded
Yersinia pestis A1122	No	excluded

#### What must be done to qualify for a clinical/ diagnostic exemption?

#### A 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 the provisions of Section 16)
  - Destroyed on-site by a recognized sterilization inactivation process
  - Retained if the entity is registered for the select agent or toxin

## What must be done to qualify for a clinical/diagnostic exemption?

#### A select or toxin must also be:

- Secured against theft, loss, or release from the time it is identified to the time it is transferred or destroyed, and reported for any theft, loss, or release
- Identification must be reported to:
  - Federal Select Agent Program within 7 calendar days of identification (diagnosis/verification) or within 90 calendar days of receipt (proficiency testing)
  - Other appropriate authorities as required by Federal, State, or local law
  - Immediate Notification for Tier 1 BSAT
- Less stringent reporting may be allowed during extraordinary circumstances, such as a widespread outbreak.

#### **APHIS/CDC Form 4 Report of Identification**

- Clinical or Diagnostic Laboratories
  - Agents used only for diagnosis, verification, or proficiency testing
- Federal law enforcement agency
  - Seizures of known select agent or toxin



Submit completed form only once by either email, fax, or mail

		SECTION A - REFER	ENCE LABOR	RATORY INFORMA	TION		
Name of individual completing Sections A and B.     First			2.	Email address:	3. Telephone	3. Telephone #.	
Registered Enfty (APHIS or CDC Registration #:  Clinical or Diagnostic Laboratory (non-registered entity (NRE))  (NRE # (provided by APHIS or CDC):			9. Enfty name:				
5. Responsible Official or Laboratory Supervisor name: First: Mit Last:		12152	10. Address (NOT a post office address):				
Telephone #.	7. Fax #	8. Email address:		11. Qly:	12. Statle	13. Zip Code	
13	SECTION B - S	ELECT AGENT OR TOXIN	IDENTIFIED I	FROM CLINICAL/D	IAGNOSTIC SPECIF	MEN(S)	
1. Select Agent or Toxin Identified				2. Date identified:			
. Case/patient/sampl	e ID #(s).	4. # of samples received:	5. Sample t	ype(s) received:	6. Casel	patient origin (zip code).	
Do you anticipate re	eceiving additional	ed under 7 CFR Part 331.19, 9 CFF samples/specimens for this case/pu er to the guidance instructions at w	atient that origina	te from the initial case (e	e.g. patient, environmenta		
		er(s)) of the specimen(s) been not and signed Sections C & D from				Yes □ N/A	
1. Comments / Notes					25 N° 347		

## What are the requirements for a provider of proficiency samples?

- At least seven calendar days prior to the transfer, the sender of the proficiency samples must report to APHIS or CDC:
  - Select agent or toxin to be transferred
  - Name and address of the recipient

## **Shipping and Receiving (Section 16)**

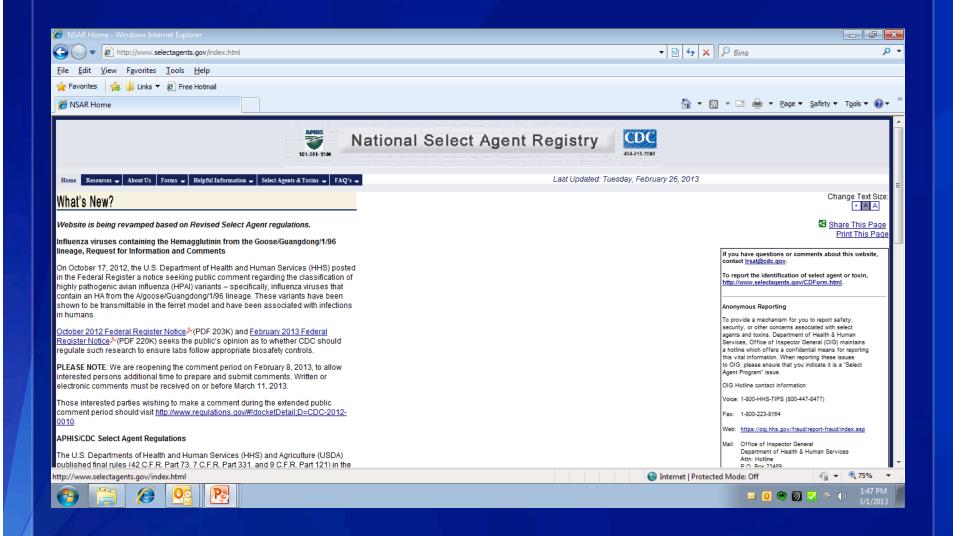
• Transportation in commerce starts when the select agent(s) or toxin(s) are packaged for shipment and ready for receipt by a courier transporting select agent(s) or toxin(s) and ends when the package is received by the intended recipient who is an individual approved by the HHS Secretary or Administrator to have access to select agents and toxins, following a security risk assessment by the Attorney General.

# **GUIDANCE**

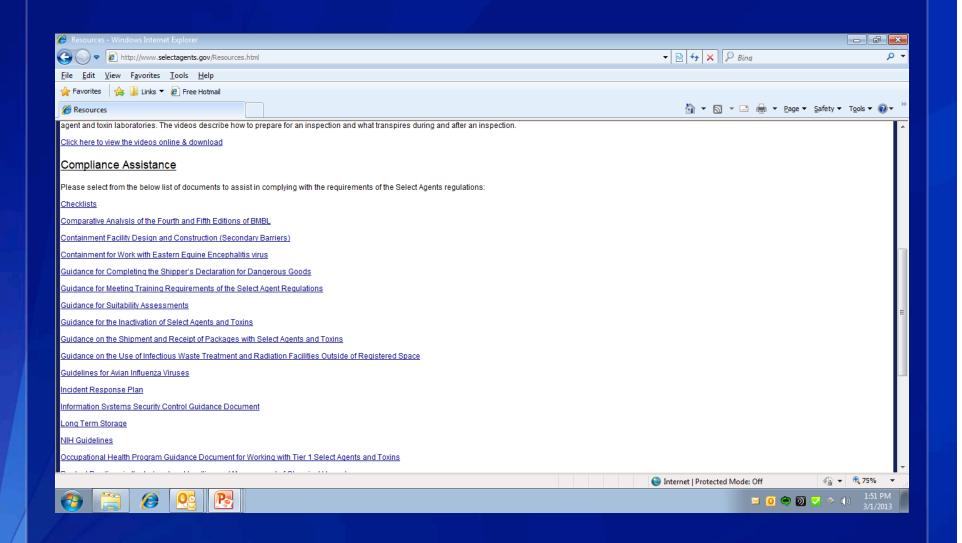
## Guidance (www.selectagents.gov)

- Frequently Asked Questions
- Incident Response
- Information Systems Security Control
- Inventory Requirements
- Long Term Storage
- Occupational Health Program
- Physical Security Control
- Responsible Official
- SA Grams
- Security Risk Assessment Tool
- Shipment and Receipt of Packages
- Suitability Assessment
- Toxin Due Diligence
- Training

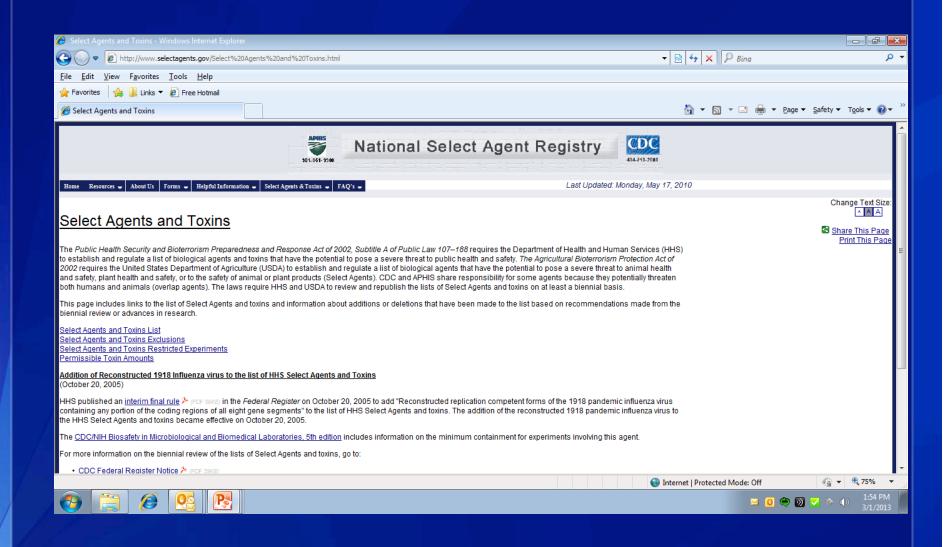
#### Tour of www.selectagents.gov



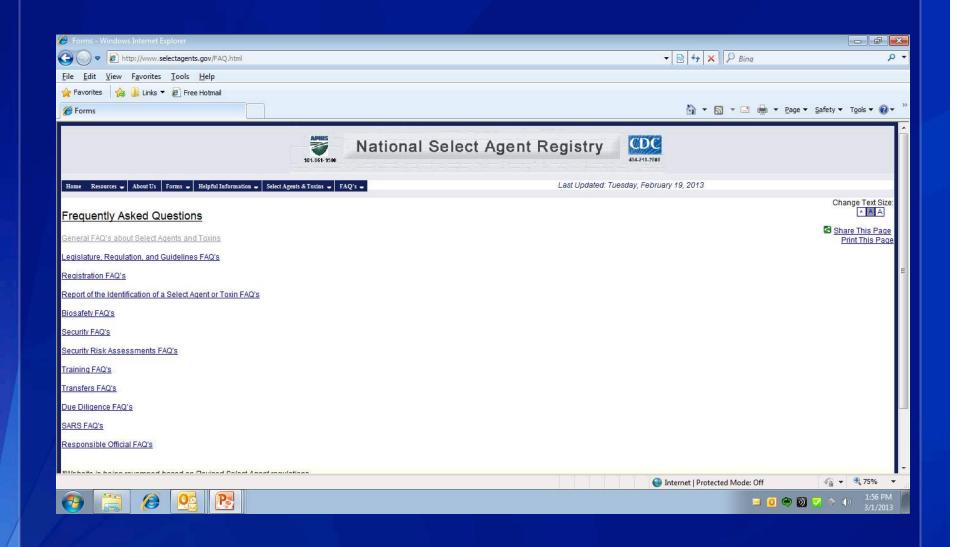
#### Resources



#### **Select Agents and Toxins**



#### **Frequently Asked Questions**



#### www.select agents.gov



For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333
Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov Web: www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

