DEPARTMENT OF HEALTH AND HUMAN SERVICES

[Docket No. CDC–2011–0012]

42 CFR Part 73

RIN 0920–AA34

Possession, Use, and Transfer of Select Agents and Toxins; Biennial Review

AGENCY: Centers for Disease Control and Prevention (CDC), Department of Health and Human Services (HHS).

ACTION: Proposed rule.

SUMMARY: In accordance with the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (the Bioterrorism Response Act), the Centers for Disease Control and Prevention (CDC) located within the Department of Health and Human Services (HHS) has reviewed the list of biological agents and toxins that have the potential to pose a severe threat to public health and safety and is proposing to amend and republish the list as required by the Bioterrorism Response Act. Further, on July 2, 2010, the President signed Executive Order 13546, ''Optimizing the Security of Biological Select Agents and Toxins in the United States'' that directed the Secretaries of HHS and Agriculture (USDA) to designate a subset of the select agents and toxins list (Tier 1) 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; explore options for graded protection for these Tier 1 agents and toxins to permit tailored risk management practices based upon relevant contextual factors; and consider reducing the overall number of agents and toxins on the select agents and toxins list. E.O. 13546 also established the Federal Experts Security Advisory Panel (FESAP) to advise the HHS and USDA Secretaries on the designation of Tier 1 agents and toxins, reduction in the number of agents on the Select Agent List, establishment of suitability standards for those having access to Tier 1 select agents and toxins, and establishment of physical security and information security standards for Tier 1 select agents and toxins. The tiering of the select agents and toxins list will allow the application of more optimized security measures for those select agents or toxins which pose a higher risk to public health and safety should they be stolen or otherwise misused.

In addition to addressing the FESAP recommendations in this Notice of Proposed Rulemaking (NPRM), we are also proposing to add two agents, Lujo and Chapare viruses to the list; adding definitions; and clarifying language concerning security, training, biosafety, and incident response. These changes will increase the usability of the select agents and toxins regulations as well as providing for enhanced program oversight.

DATES: Comments should be received on or before December 2, 2011.

ADDRESSES: You may submit comments, identified by Regulatory Information Number (RIN), 0920–AA34 in the heading of this document by any of the following methods:

- *Federal eRulemaking Portal: http://www.regulations.gov.* Follow the instructions for submitting comments.
- *Mail:* Centers for Disease Control and Prevention, Select Agent Program, 1600 Clifton Road, NE., Mailstop A–46, Atlanta, Georgia 30333, *Attn:* RIN 0920–AA34.

Instructions: All submissions received must include the agency name and RIN for this rulemaking. All relevant comments received will be posted without change to *http://www.regulations.gov,* including any personal information provided.

Docket Access: For access to the docket to read background documents or comments received or to download an electronic version of the NPRM, go to *http://www.regulations.gov.* Comments will be available for public inspection Monday through Friday, except for legal holidays, from 9 a.m. until 5 p.m. at 1600 Clifton Road, NE., Atlanta, GA 30333. Please call ahead to 1–866–694–4867 and ask for a representative in the Division of Select Agents and Toxins to schedule your visit. Our general policy for comments and other submissions from members of the public is to make these submissions available for public viewing on the Internet as they are received and without change.

FOR FURTHER INFORMATION CONTACT: Robbin Weyant, Director, Division of Select Agents and Toxins, Centers for Disease Control and Prevention, 1600 Clifton Road, NE., Mailstop A–46, Atlanta, Georgia 30333. *Telephone:* (404) 718–2000.

SUPPLEMENTARY INFORMATION: The Preamble to this notice of proposed rulemaking is organized as follows:

I. Background

The Public Health Security and Bioterrorism Preparedness and Response Act of 2002, Subtitle A (Department of Health and Human Services) of Title II (Enhancing Controls on Dangerous Biological Agents and Toxins) of Public Law 107–188 (June 12, 2002) (42 U.S.C. 262a) (the Bioterrorism Response Act), requires the HHS Secretary to establish by regulation a list of each biological agent and each toxin that has the potential to pose a severe threat to public health and safety. In determining whether to include an agent or toxin on the list, the HHS Secretary considers the effect on human health of exposure to an agent or toxin; the degree of contagiousness of the agent and the methods by which the agent or toxin is transferred to humans; the availability and effectiveness of pharmacotherapies and immunizations to treat and prevent illnesses resulting from an agent or toxin; the potential for an agent or toxin to be used as a biological weapon; and the needs of children and other vulnerable populations. The current list of HHS select agents and toxins can be found at 42 CFR 73.3 (HHS select agents and toxins) and 42 CFR 73.4 (Overlap select agents and toxins). The list of HHS and Overlap select agents and toxins is available at: *http://www.selectagents.gov/Select%20Agents%20and%20Toxins%20List.html.* The Bioterrorism Response Act requires that the HHS Secretary review and republish the list of select

agents and toxins on at least a biennial basis. See 42 U.S.C. 262a(a)(2).

The HHS Secretary last republished the HHS select agents and toxins list in the **Federal Register** on October 16, 2008 (73 FR 61363). The HHS select agents and toxins list is divided into two sections. The select agents and toxins listed in § 73.3 (HHS select agents and toxins) are those regulated only by HHS under the authority of the Bioterrorism Response Act. The select agents and toxins listed in § 73.4 (Overlap select agents and toxins) are those regulated by HHS under the authority of the Bioterrorism Response Act and regulated by the USDA under the authority of the Agricultural Bioterrorism Protection Act of 2002 (7 U.S.C. 8401).

To fulfill this statutory mandate, the Center for Disease Control and Prevention's (CDC) Division of Select Agents and Toxins (DSAT) initiated its biennial review process, which included consultation with CDC's Intragovernmental Select Agents and Toxins Technical Advisory Committee (ISATTAC) and other subject matter experts. The ISATTAC is comprised of Federal government employees from the CDC, the National Institutes of Health (NIH), the Food and Drug Administration (FDA), the USDA/Animal and Plant Health Inspection Service (APHIS), USDA/Agricultural Research Service (ARS), USDA/CVB (Center for Veterinary Biologics), the Department of Homeland Security (DHS), the Department of Defense (DOD), and the Biomedical Advanced Research and Development Authority (BARDA) within the Office of the Assistant Secretary for Preparedness and Response in HHS.

CDC also published an ANPRM in the **Federal Register** (75 FR 42363) (July 21, 2010 ANPRM) inviting comments concerning potential changes to part 73 of Title 42 of the Code of Federal Regulations (the select agent regulations). We solicited comments regarding (1) the appropriateness of the current HHS list of select agents and toxins; (2) whether there are other biological agents or toxins that should be added to the HHS list; (3) whether biological agents or toxins currently on the HHS list should be deleted from the list; (4) whether the HHS select agents and toxins list should be tiered based on the relative bioterrorism risk of each biological agent or toxin; and (5) whether the security requirements for select agents or toxins in the highest tier should be further stratified based on type of use or other factors. We requested recommendations regarding the criteria to use to designate high risk select agents and toxins and those recommendations were included in the interagency working group discussions on the matter. Relevant issues raised by the comments are discussed below in ''II. Proposed Changes to 42 CFR part 73.''

On July 2, 2010, President Obama signed Executive Order (E.O.) 13546: ''Optimizing the Security of Biological Select Agents and Toxins in the United States'' that directed the Secretaries of HHS and USDA to (1) designate a subset of the select agents and toxins list (Tier 1) 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; (2) explore options for graded protection of Tier 1 agents and toxins to permit tailored risk management practices based upon relevant contextual factors; and (3) consider reducing the overall number of agents and toxins on the select agents and toxins list. E.O. 13546 also established the FESAP to advise the HHS and USDA Secretaries on the designation of Tier 1 agents and toxins, reduction in the number of agents on the Select Agent List, establishment of personnel reliability standards for those having access to Tier 1 select agents and toxins, and establishment of physical security and information security standards for Tier 1 select agents and toxins. E.O. 13546 is available at: *http://edocket.access.gpo.gov/2010/pdf/2010-16864.pdf.* The FESAP provided its recommendations to the HHS and USDA Secretaries on November 2, 2010. The FESAP recommendations addressed the reduction of the list of select agents and toxins, the identification of a subset of the list that includes those 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; and the optimization of security programs at registered entities. In drafting its recommendations to modify and stratify the list of select agents and toxins, the FESAP utilized expert knowledge of the agents, combined with information from the DHS's Material Threat Determinations of biological agents and toxins. Care was used to balance risks identified with the Congressional mandate to ensure the availability of select agents and toxins for research and educational activities.

Other sources of input that we have considered in the drafting of this Proposed Rule include the following: The National Science Advisory Board for Biosecurity, the National Academies, and comments received from professional societies and the public in response to the CDC ANPRM published on July 21, 2010.

The purpose of this notice of proposed rulemaking is to seek public comment on (1) the appropriateness of the current HHS and Overlap list of select agents and toxins including whether there are other agents or toxins that should be added to the HHS or Overlap list or whether agents or toxins currently on the HHS or Overlap list should be deleted from the list; (2) the appropriateness of the proposed tiering of the select agents and toxins list; (3) whether minimum standards for personnel reliability, physical and cyber security should be prescribed for identified Tier 1 agents; and (4) any other aspect of the proposed amendments to the select agent regulations.

II. Proposed Changes to 42 CFR Part 73

PROPOSED CHANGES TO 42 CFR PART 73

Section No.	Current	Change
73.0	Applicability and related requirements	No change.
73.1	Definitions	Definitions added: Adjudicated as a mental defective; alien; committed to any mental institution; controlled substance; crime punishable by imprisonment for a term exceeding 1 year; indictment; information security; lawfully admitted for permanent residence; mental institution; occupational exposure; recombinant and synthetic nucleic acids; restricted person; unlawful use of any controlled substance.
73.2	Purpose and scope	No change.
73.3	HHS select agents and toxins	Designates Tier 1 select agents and toxins; adds select agents and toxins; clarifies language; deletes from the HHS list.

PROPOSED CHANGES TO 42 CFR PART 73—Continued

Section No.	Current	Change
73.4	Overlap select agents and toxins	Designates Tier 1 select agents and toxins; adds select agents and toxins; clarifies language; deletes from the overlap list.
73.5	Exemptions for HHS select agents and toxins.	Amends the immediate notification list to Tier 1 agents.
73.6	Exemptions for overlap select agents and toxins.	Amends the immediate notification list to Tier 1 agents.
73.7	Registration and related security risk assessments.	No change.
73.8	Denial, revocation, or suspension of registration.	Clarifies language.
73.9	Responsible Official	Redesignates paragraphs; adds new paragraphs (a)(3), (a)(6).
73.10	Restricting access to select agents and toxins; security risk assessments.	Redesignates paragraphs; adds new paragraph (e); adds clarifying language.
73.11	Security	Revises regulatory text—paragraph (b), (c)(2). Redesignates paragraphs; adds new paragraphs (c)(8), (c)(9), (c)(10), (e).
73.12	Biosafety	Revises paragraphs (a) and (c)(1); replaces ''url'' in paragraph (c)(3); redesignates paragraph (d); adds new paragraph (d).
73.13	Restricted experiments	Clarifies language.
73.14	Incident response	Redesignates paragraphs; adds new paragraphs (d) and (e).
73.15	Training	Revises paragraph (a); redesignates paragraphs; adds new paragraph (b).
73.16	Transfers	Redesignates paragraphs; adds new paragraphs (f), (h), (l).
73.17	Records	Revises paragraph (a)(1); redesignates paragraphs; adds new paragraph (a)(2).
73.18	Inspections	No changes.
73.19	Notification of theft, loss, or release	No changes.
73.20	Administrative review	Revises paragraphs.
73.21	Civil money penalties	No changes.

A. Modifications to the List of HHS Select Agents and Toxins

The following changes to the list of HHS select agents and toxins are proposed based on comments received in response to the July 21, 2010 ANPRM, recommendations from the FESAP and ISATTAC, and our review of current scientific data regarding select agents and toxins. As we discuss below, we are proposing to remove 6 select agents, add 2 select agents, and identify 11 select agents and toxins as ''Tier 1'' agents to the HHS list of select agents and toxins.

Proposed Addition of Lujo and Chapare Viruses

On August 19, 2009 (74 FR 41829), we proposed the addition of Chapare virus to the HHS list of select agents and toxins; we did not receive any comments regarding that proposal. Based on scientific data and risks associated with this virus, the ISATTAC recommended the addition of Chapare virus to the HHS list of select agents and toxins. The determination to add Chapare virus to the HHS list of select agents and toxins was based on the following scientific information. The HHS list currently includes members of the *arenaviridae* family (Junin, Machupo, Sabia, Flexal, Guanarito, and Lassa). Arenaviruses are rodent-borne viruses, some of which can be associated with large hemorrhagic fever outbreaks, and untreated case fatalities can be in excess of 30 percent. Chapare virus is a recently described New World arenavirus that is associated with fatal hemorrhagic fever syndrome and is most closely related to Sabia virus, an HHS select agent (Ref 1). Based on the ISATTAC recommendation and our examination of the current scientific data and risks associated with this virus, we are proposing to add Chapare to the HHS list.

The ISATTAC also recommended the addition of Lujo virus to the HHS list of select agents and toxins. Based on this recommendation and our examination of the current scientific data and risks associated with this virus, we are also proposing to add Lujo virus. The scientific determination was based on the fact that the Lujo virus caused a fatal outbreak of hemorrhagic fever, has an unprecedented high case fatality rate of 80 percent, has been phylogenetically identified as an arenavirus and is related to those members of the Old World *arenaviridae* family (Junin, Machupo, Sabia, Flexal, Guanarito, and Lassa) listed as HHS select agents that cause hemorrhagic fever and pose a significant risk to public health and safety (Ref 2).

Proposed Removal of Cercopithecine Herpesvirus 1 (Herpes B Virus)

Commenters acknowledged in response to the July 21, 2010 ANPRM that (1) the Herpes B virus naturally infects many species of macaques; and (2) can produce a serious, often fatal, infection in humans when not treated. However, the commenters argued that Herpes B virus should not be included as a select agent based on the following assertions:

- The inclusion of the virus on the list will produce no significant improvements in safety for the American public.
- Given the high prevalence of infection in non-human primates and the relatively few human infections that have been recorded, it suggests that the virus is not easily transmitted to humans.
- The virus is capable of being treated with several available licensed antiviral compounds.
- The virus does not present a sufficient risk of infection by the aerosol route.
- The virus is a highly unlikely candidate for a bioterrorism agent due to its environmental instability and the need for direct contact for infection. The argument is further enhanced by the absence of the virus listed on the NIH's National Institute of Allergy and Infectious Diseases lists of Category A, B & C Priority Pathogens or the CDC's Category A, B & C Bioterrorism Agents lists.
- The virus is widely available in nature.

The ISATTAC and the FESAP also recommended the removal of Cercopithecine herpesvirus 1 (Herpes B virus) from the HHS list of select agents and toxins. We agreed with the

commenters, ISATTAC, and FESAP and propose to remove Cercopithecine herpesvirus 1 (Herpes B virus) from the HHS list of select agents and toxins. Our rationale for this proposal is based on the facts that this virus is not easily transmitted to humans, the person-to-person transmission risk is small, the numbers of recorded human infections are low, and multiple licensed antiviral treatments for Herpes B infections are available.

Proposed Removal of *Coccidioides posadasii/Coccidioides immitis*

Commenters to our July 21, 2010 ANPRM argued that *Coccidioides posadasii/Coccidioides immitis* should not be included as a select agent based on the following reasons:

- The characteristics of *Coccidioides* species do not provide convincing properties of an effective agent of bioterrorism.
- The fungi are endemic in the southwestern United States, but do not cause large epidemics even with high prevalence in the air during wind storms.
- Infections caused by the fungi are easily treatable by licensed antifungal medicines, especially early in disease.
- The difficulty to use *Coccidioides* species as a bioweapon, and hence the need for strict regulation under the select agent regulations, is exemplified by their non-communicability, lack of history of use or development as successful biological weapons, and a relatively low incidence of symptomatic disease following natural infection.
- *Coccidioides* species would not be an effective bioterrorism weapon because the percentage of deaths and hospitalizations are low considering the number of people infected.

The FESAP also recommended removal of *Coccidioides posadasii/Coccidioides* immitis from the HHS list of select agents and toxins. We agreed with the commenters and FESAP and propose to remove *Coccidioides posadasii/Coccidioides* immitis from the HHS list of select agents and toxins. The scientific determination was based on the availability of licensed treatments for *Coccidioides* infection and a lowering of our assessment of the impact of *Coccidioides* infection on human health, as indicated by the high proportion of subclinical cases observed in endemic areas (Ref 3).

Proposed Retention of *Coxiella burnetii*

Commenters to the July 21, 2010 ANPRM argued that *Coxiella burnetii* (Q fever) should be removed from the select agents and toxins list based on the following assertions:

- Q fever is not contagious and is effectively treated with licensed antibiotics.
- It is generally a self-limiting infection with potential control by licensed vaccination.
- The ubiquitous nature of *Coxiella burnetii* means that it can be easily acquired from environmental sources and calls into question the effectiveness and procedures for maintaining inventories of select agents.
- Person-to-person transmission of the disease is rare and is fatal less than one percent of the time.
- A vaccine is available for this agent internationally, but not domestically.
- The agent is commonly found in animal populations within the United States.

However, FESAP and ISATTAC did not recommend removing this bacterium from the HHS list of select agents and toxins. We agreed with the FESAP and ISATTAC recommendations and propose to retain *Coxiella burnetii* on the HHS select agents and toxins list. The determinations to retain this agent on the HHS list are its robust environmental stability, ease of transmission to humans, extremely low infectious dose, and prior association of this agent with offensive programs. CDC invites comments regarding retaining this agent on the HHS list of select agents and toxins.

Proposed Removal of South American Genotypes of Eastern Equine Encephalitis Virus (EEEV)

Commenters on the July 21, 2010 ANPRM regarding the proposed inclusion of EEEV on the list of select agents and toxins argued that EEEV should not be included as a select agent based on the following reasons:

- The virus occurs naturally in the environment.
- Direct person-to-person transmission does not occur.
- Local and State health departments and mosquito control agencies routinely release information regarding the location of arboviral activity in the community, so upholding strict biosecurity measures in a laboratory has little or no impact on reducing a terrorist's ability to acquire this agent.
- Only North American strains of EEEV should be regulated because transmission patterns limit the distribution and epidemic potential of South American strains, which are less pathogenic.

We examined the current scientific data and noted that strains of EEEV can be categorized into two distinct genotypes primarily based upon geographic distribution: North American genotype (NA EEE) and South American genotype (SA EEE). The NA EEE genotype consists of strains obtained from North America and the Caribbean while SA EEE genotype viruses originate in Central and South America. Viruses in the two genotypes are distinctly different in their genetics, epidemiology, and pathogenicity. NA EEE, which are the strains responsible for human and equine disease, are all genetically very similar to each other (less than 3% divergence at the nucleotide level) and can be easily distinguished from SA EEE genotype strains by sequencing. NA EEE genotype strains differ from SA EEE viruses by greater than 20% at the nucleotide level and approximately 10% at the amino acid level. Since FESAP agreed with our scientific assessment that SA EEE genotypes should be removed from the HHS list of select agents and toxins, we are proposing to remove SA EEE genotypes from the HHS list of select agents and toxins (Ref 4).

Proposed Removal of Flexal Virus

Commenters that responded to the July 21, 2010 ANPRM felt that Flexal virus should be removed from the HHS list of select agents and toxins based on the lack of severity of disease and the lack of significant outbreaks of disease associated with infection with this virus in humans. FESAP also recommended that Flexal virus be removed from the list. Since our research found a lack of significant outbreaks of disease associated with Flexal virus in humans and that this virus would be a highly unlikely candidate for a bioterrorism agent, we are proposing to remove Flexal virus from the HHS list of select agents and toxins.

Proposed Retention of Monkeypox Virus

Commenters to the July 21, 2010 ANPRM recommended that Monkeypox virus should not be included as a select agent based on the following assertions:

- An effective licensed vaccine is available.
- Promising antivirals are in advanced stages of development.
- The virus is inefficiently transmitted from person-to-person.

We examined the current scientific data and noted that there is an increased incidence of Monkeypox virus in humans as well as studies identifying the virus being easily transmitted in Gambian rats. A recent study on an outbreak in Sudan indicates there is much strain variation in level of infectivity and severity of disease. Concern over the detection of new lineages with increased pathogenesis has been expressed. Another recent

outbreak of Monkeypox virus in the United States suggested numerous animals could become infected complicating the understanding of zoonotic maintenance of the virus (Ref 29–33).

While there has been documented cross protection against Monkeypox virus by Vaccinia virus vaccine, the decrease in the number of individuals with any immunity to the virus is drastically declining (since smallpox vaccination no longer occurs). Further, even though there is a stockpile of Vaccinia virus vaccine available, the vaccine has numerous undesirable side-effects that make it less than optimal for mass vaccination. There are also several antiviral treatments for Monkeypox in advanced stages of development, but they are not currently available. Thus, there is currently no specific treatment (Ref 29–33).

FESAP recommended keeping Monkeypox virus on the HHS list of select agents and toxins.

Based on the scientific determination outlined above, we are proposing to retain Monkeypox virus on the HHS list of select agents and toxins. We will continue to monitor progress in the development of antivirals and other means of prevention and control of Monkeypox virus infections and invite comments on removing a certain clade of Monkeypox virus (i.e., West African clade of Monkeypox virus) from the HHS list of select agents and toxins.

Proposed Reorganization of Tick-Borne Encephalitis Complex Viruses (TBEV)

Even though we received no comments to the July 21, 2010 ANPRM regarding the removal of these viruses from the HHS list of select agents and toxins, we are proposing the removal of TBEV Central European subtype from the HHS list of select agents and toxins for the following scientific reasons:

- The TBEV Central European Tick-borne subtype has been shown to be less virulent in humans than the Far Eastern subtype (Ref 5).
- No TBEV vaccines are licensed or available in the United States; however two safe, effective inactivated TBEV vaccines are available internationally.

FESAP also recommended the removal of the TBEV Central European subtype from the HHS list of select agents and toxins.

In addition to removing the TBEV Central European subtype from the HHS list of select agents and toxins, we propose to reorganize the listing of the TBEV to reflect the current nomenclature given by the International Committee on Taxonomy of Viruses. For TBEV proper, there are now just three recognized subtypes: Central European, Far Eastern, and Siberian. The Russian Spring and Summer encephalitis designation is no longer recognized (Ref 6). Two other viruses on the HHS list of select agents and toxins, Kyasanur Forest disease virus and Omsk Hemorrhagic fever virus, are no longer classified as TBEV. In recognition of these taxonomic changes, we are proposing to include these viruses on the HHS list of select agents and toxins as follows:

Tick-borne encephalitis virus
  Far Eastern subtype
  Siberian subtype
Kyasanur Forest disease virus
Omsk Hemorrhagic fever virus

Proposed Retention of *Rickettsia prowazekii* and *Rickettsia Rickettsii*

Commenters that responded to the July 21, 2010 ANPRM argued that *Rickettsia prowazekii* and *Rickettsia rickettsii* should be removed from the HHS list of select agents and toxins based on the following assertions:

- Mimicking transmission by arthropod vectors in an effort to disperse these pathogens with the intent to disrupt society would be challenging and technologically unlikely to be successful.
- Common and readily available licensed antibiotics are highly effective, and contagion is not a threat because spread is determined by contact with the vectors, not through person-to-person contact.
- Although *Rickettsia prowazekii* may be a pathogen of military significance, *Rickettsia rickettsii* is not. According to the commenter, propagation of the pathogens requires growth in cultured host cells and natural infection occurs by parenteral inoculation through a tick vector, so mass exposure by aerosolization or contamination of food sources is unlikely to result in disease.
- The potential to use this agent as a platform to construct a genetically engineered new pathogen would be extremely difficult.
- The primary disease associated with *Rickettsia rickettsii* is Rocky Mountain Spotted Fever, and the symptoms are recognizable and marketed diagnostics and treatment are readily available.
- *Rickettsia rickettsii* should be removed because generation of even moderate amounts of infectious material is exceedingly difficult and requires specialized equipment.
- Rickettsiae are not spread directly from person-to-person, would not survive if dispersed into the environment, and are susceptible to a number of readily available licensed antibiotics. In addition, there is no possibility of eliminating their presence in the environment.
- Potential benefits of lessening restriction on research include improved diagnostic capabilities and better potential for vaccine development.

The FESAP and ISATTAC recommended keeping *Rickettsia prowazekii* and *Rickettsia rickettsii* on the HHS list of select agents and toxins. Since we agreed with these expert panels, we are proposing to retain *Rickettsia prowazekii* and *Rickettsia rickettsii* on the HHS select agents and toxins list based on our scientific determination regarding the environmental stability, low infectious dose, aerosol transmission, and clinical significance of infection with these organisms.

Proposed Retention of *Yersinia pestis*

Commenters that responded to the July 21, 2010 ANPRM argued that *Yersinia pestis* should not be included as a select agent based on the following assertions:

- *Yersinia pestis* is naturally occurring and does not survive for long outside of its rodent host because of susceptibility to heat and sunlight.
- Decontamination of surfaces is highly effective in limiting its spread.
- Licensed treatments are readily available for those who may become exposed.

The FESAP and ISATTAC recommended that *Yersinia pestis* remain on the HHS list of select agents and toxins.

We agree with the FESAP and ISATTAC, and are proposing to keep *Yersinia pestis* on the HHS select agents and toxins list based on our scientific conclusion regarding the bacterium's high mortality rate, ease of dissemination and production, and person-to-person transmission of *Yersinia pestis* infections.

Proposed Reorganization of Staphylococcal Enterotoxins

Commenters to the July 21, 2010 ANPRM suggested that the regulations needed a clear statement concerning staphylococcal enterotoxins (SEs) and staphylococcal enterotoxin-like toxins (SEls). Commenters stated that SEs and SEls have been distinguished from each other on the basis of emetic activity (Ref 12). Commenters were confused regarding whether the intent of the select agent regulations is to acknowledge this difference and not regulate SEls or to regulate both SEs and SEls.

ISATTAC recommended that we amend the HHS list of select agents and toxins to specifically include Staphylococcal enterotoxins A, B, C, D, and E in the HHS list of select agents and toxins. We agree with the commenters and the ISATTAC recommendation, and propose to amend the select agents and toxins list from ''Staphylococcal enterotoxins'' to specifically include ''Staphylococcal enterotoxins A, B, C, D, and E'' in the HHS list of select agents and toxins (Ref 7–14). Serotypes G, H, and I should not added to the HHS list of select agents and toxins because serotypes G, H, and I are at least 10 fold less of a risk than SEE and SEA (Ref 15–16.) According to the International Nomenclature Committee for Staphylococcal Superantigens, emesis in a primate model within five hours post-feeding must be observed to classify an exotoxin as an enterotoxin (Ref 12). If emesis is not observed in this period of time, the exotoxin should be classified as enterotoxin-like rather than enterotoxin. Based on this internationally accepted standard, we are proposing serotypes J, K, L, M, N, O, P, Q, T, U, U2 and V should be designated staphylococcal enterotoxin-like rather than enterotoxin because these serotypes have been shown to either not cause emesis in a primate model or have not been tested for emesis (Ref 17–26). Therefore, we are proposing serotypes J, K, L, M, N, O, P, Q, T, U, U2 and V should not added to the HHS list of select agents and toxins.

B. Modifications to the List of Overlap Select Agents and Toxins

The following changes to the list of Overlap select agents and toxins are proposed based on comments received to the July 21, 2010 ANPRM, recommendations from the FESAP and ISATTAC, and our review of current scientific data regarding select agents and toxins.

Proposed Retention of *Bacillus anthracis* (Pasteur Strain)

A commenter to the July 21, 2010 ANPRM stated that the Pasteur strain of *Bacillus anthracis* should not be considered a select agent because the strain is attenuated and used for quality control testing in Laboratory Response Network (LRN) laboratories. The commenter argued that changing the status of the Pasteur strain would alleviate the burden of recordkeeping for quality control and proficiency testing activities.

We made no changes based on this comment. It should be noted that we excluded *Bacillus anthracis* Sterne strain in 2003 because the attenuated strain was determined to not pose a severe threat to public health and safety, animal health, or animal products. We have not excluded the plasmid-negative Pasteur variant in order to prevent the combination of plasmids from Sterne and Pasteur-types of strains to create a wild type phenotype.

Proposed Retention of *Brucella abortus, Brucella melitensis,* and *Brucella suis*

Commenters to the July 21, 2010 ANPRM recommended that *Brucella abortus, Brucella melitensis,* and *Brucella suis* be removed from the Overlap list of select agents and toxins for the following reasons:

- The benefits of removal far exceed any risk mitigated by continuing the listing. In the years since the organism was first listed, research and development has been greatly diminished.
- As currently regulated, existing BSL–3 facilities do not have the capacity to conduct brucellosis research with sufficient numbers of animals to generate statistically valid research results, and it is too expensive to construct and maintain enough high capacity BSL–3 facilities to conduct the necessary research. The commenter contended that any risk currently mitigated by the listing is fully manageable without such listing.
- *Brucella abortus* and *Brucella suis* should be removed because the organisms are adversely affected by environmental conditions and can be diagnosed and controlled in animals and readily treated in humans. The classification of these bacteria as select agents has hampered research that could result in vaccines that would protect susceptible animal populations. Although brucellosis will remain a disease of agricultural significance, *Brucella abortus* and *Brucella suis* are not ideal biological weapons. The commenter suggested, however, that *Brucella melitensis* remain on the list because it is a foreign animal disease and the most infectious of all the species.
- *Brucella* species should have their listed status reconsidered because human infection is rarely fatal, acute brucellosis can be readily treated with available antibiotics, human-to-human transmission is extremely rare, and wildlife carriers in the United States often come into contact with humans without significant transmission.
- Naturally occurring substances such as *Brucella* should be removed because infections regularly occur from natural exposures.
- The primary mode of transmission for *Brucella* abortus is through contact with contaminated fluids/tissues, its pathogenicity is moderate, and infections are routinely treated with antibiotics that do an effective job. The commenter recommended removal of *Brucella abortus* strain 1119–3 because the strain is identical using conventional typing tests to strain 19 and is used as an antigen strain in diagnostic tests. Strain 19 and RB51 have been excluded as licensed vaccine products, but other research strains have not been excluded.
- Another commenter supported downgrading the risk assessment for vaccine strains of *Brucella.* The commenter was concerned that the only criterion the ISATTAC accepts for exclusion is licensed drug status, but such a high standard is disadvantageous to research on this pathogen.

The FESAP and ISATTAC recommended that *Brucella abortus, Brucella melitensis,* and *Brucella suis* remain on the Overlap list of select agents and toxins. We made no changes based on these comments because we agreed with these expert panels that *Brucella abortus, Brucella melitensis,* and *Brucella suis* remain on the Overlap list of select agents and toxins based on the bacteria's ease of production, high infectivity via the aerosol route, low infectious dose, and no brucellosis vaccines are currently available for humans in the United States.

Proposed Retention of *Burkholderia mallei* and *Burkholderia pseudomallei*

Commenters to the July 21, 2010 ANPRM contended that *Burkholderia mallei* and *Burkholderia pseudomallei* should not be included as select agents based on the following reasons:

- The agents do not rise to the same level of public health threat or feasibility for weaponization that the other agents on the list do.
- *Burkholderia mallei* and *Burkholderia pseudomallei* are endemic in a number of areas of the world.
- Disease resulting from *Burkholderia mallei* and *Burkholderia pseudomallei* is treatable with low mortality.
- It is questionable how they would be used as bioweapons.

The FESAP and ISATTAC recommended that *Burkholderia mallei and Burkholderia pseudomallei* remain on the Overlap list of select agents and toxins. We made no changes based on these comments because we agreed with these expert panels that *Burkholderia mallei and Burkholderia pseudomallei* should remain on the Overlap list of select agents and toxins based on our scientific determination that the bacteria

can be produced in large quantity; transmitted via aerosol; and *Burkholderia pseudomallei* is highly stable in the environment. The mortality rate for untreated cases of both melioidosis and glanders is high, and given the rarity of these diseases in the United States, experience in their diagnosis and treatment is limited.

Proposed Reorganization of Venezuelan Equine Encephalitis Virus (VEEV)

Commenters to the July 21, 2010 ANPRM contended that VEEV subtypes ID and IE should not be included as select agents based on the following reasons:

- Inclusion of VEEV subtypes as select agents should be based solely on their ability to cause an epidemic or epizootic following a bioterrorism event. This would require inclusion of only varieties 1AB and 1C VEEV which have been shown to have epidemic/epizootic potential.
- The reasons for excluding 1D and 1E VEEVs from the select agent list are: (1) No subtype 1D or 1E VEEV have ever caused large equine epizootics; (2) Inclusion of 1D viruses because they might be precursors to 1C viruses is not sufficient for making 1D viruses select agents. Essentially all of this evidence is laboratory based. The possibility of a 1D virus mutating to a 1C virus following a bioterrorism event is unlikely because 1D viruses are unlikely to establish epidemic or epizootic transmission cycles in the US. Natural transmission cycles would likely be needed for any evolution from 1D to 1C to occur in nature; (3) Emergency vaccination of equines with currently approved equine vaccines or humans with IND vaccines (e.g. TC–83) would interdict or greatly dampen a 1D or a 1E epizootic, based on antigenic cross-reactivities of subtype 1 viruses; and (4) The currently available humanized or human anti-VEEV monoclonal antibodies that could be produced for emergency use would also have prophylactic, and possibly therapeutic efficacy for all VEEV subtype 1 infections with which they cross react (includes 1D and 1E viruses).

The FESAP and ISATTAC recommended removal of certain subtypes of Venezuelan equine encephalitis virus from the Overlap list of select agents and toxins. Since we agreed with commenters and expert panels recommendations, we are proposing to clarify that only VEEV subtypes IAB and IC should remain on the Overlap list of select agents and toxins because these subtypes contain the only recognized strains of Venezuelan equine encephalitis that have demonstrated the ability to cause epidemics or epizootics. The remaining subtypes, ID and IE, are strains prevalent among the existing animal populations and do not represent the same type of risk. Other viruses within the Venezuelan equine encephalitis complex (subtypes IF and II through IV) are separate viruses and are not included in the HHS and USDA overlap list of select agents and toxins.

C. Tiering

E.O. 13546 specifies that a subset of the Select Agent List be categorized as ''Tier 1'' because these agents and toxins present 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. All but one of the commenters to the July 21, 2010 ANPRM who addressed the idea of a tiering system based on the relative bioterrorism risk of each agent or toxin favored the use of tiers. Several commenters mentioned specific criteria for tiering. A few commenters expressed the concern that tiering could create confusion, especially for facilities with multiple Biological Select Agents and Toxins (BSAT) and had concerns about additional requirements that would be placed on some laboratories. Some commenters identified specific Tier 1 candidates from the BSAT listed in 42 CFR 73.3 and § 73.4. Most of these commenters included Variola major virus and Variola minor virus, as well as Reconstructed 1918 Influenza virus, Ebola viruses, and Marburg virus in their Tier 1 list. Two commenters also suggested *Bacillus anthracis* and Lassa fever virus. Other commenters suggested *Francisella tularensis,* South America hemorrhagic fever viruses, *Brucella* species, *Coxiella burnettii,* Botulinum neurotoxin, and Ricin as candidates for Tier 1.

Based on E.O. 13546, a FESAP recommendation and our agreement with the comments received, we are proposing to amend the select agent regulations to establish a number of select agents and toxins as Tier 1 select agents and toxins within the lists of HHS and Overlap select agents and toxins. All select agents and toxins were scored against 20 criteria by over 60 Subject Matter Experts representing the Federal life sciences, public health, law enforcement, security, and intelligence communities, which included:

- The relative ease with which a particular select agent or toxin might be disseminated or transmitted from one human to another or into the environment where it could produce a deleterious effect upon human health;
- The potential for a high mortality rate;
- The potential for a major human health impact;
- Select agents or toxins whose misuse might result in public panic or other social or economic disruption; and
- Select agents or toxins whose use might require Federal, State, and/or local officials to take special action in planning for major human health disasters.

The select agents that we propose will be designated as Tier 1 are the following:

HHS

- Ebola virus
- *Francisella tularensis*
- Marburg virus
- Variola major virus
- Variola minor virus
- *Yersinia pestis*
- Botulinum neurotoxin
- Toxin-producing strains of *Clostridium botulinum*

OVERLAP

- *Bacillus anthracis*
- *Burkholderia mallei*
- *Burkholderia pseudomallei*

Regarding the Reconstructed 1918 Influenza virus, recent studies have increased our understanding of the public health risks associated with this agent. Current reports indicate that 60 percent of the population in the United States is immune to the 1918 Influenza virus and that antiviral treatments exist (Ref 27–28). Based on this information we propose to retain the Reconstructed 1918 Influenza virus on the HHS list of select agents and toxins, but not to include it in Tier 1 of this list.

Based on the information currently available, we conclude that the adoption of the Tier 1 designation would not result in significant economic effects to the regulated community. However, we are asking for any additional data or comments on the potential effects of designating the above agents as Tier 1.

D. Responses to Other Comments and Other Proposed Changes

With respect to the remainder of the sections outlined below, we are proposing the following changes based on comments received in response to the July 21, 2010 ANPRM and recommendations from the FESAP. We are proposing to update the Web address throughout the document as all information concerning the Federal Select Agent Program is now centralized on the National Select Agent Registry Web site at *http://www.selectagents.gov/*. We also are proposing non-substantive changes throughout the

regulations for purposes of clarity. In addition, HHS/CDC and USDA/APHIS made the language similar to ensure consistency between the regulations.

Exclusions

In order to update the regulations to accurately reflect the way in which we handle the listing of exclusions, we are proposing to remove the language stating that exclusions will be published in the **Federal Register**. This change is necessary because, while we anticipated publication of exclusions both in the **Federal Register** and on the Internet at the time the regulations were initially created, we have found that publication on the select agent Web site only has served to provide the most up-to-date information to the regulated community.

Security

Commenters that responded to the July 21, 2010 ANPRM suggested security requirements include laboratory handling only by certified, trained individuals; physical security systems; restricted access; and security risk assessments. Commenters also identified some criteria for stratifying, such as making the requirements risk-based, considering the type of work done at the facility, acknowledging that many threats are from disgruntled insiders, requiring review of the stratification by subject matter experts, and taking into account the needs of the researchers at the facility.

Based on our agreement with the comments received, and input from the FESAP and stakeholder groups, we are proposing more specific minimum security standards for Tier 1 select agents or toxins. These additional requirements would be added as section 73.11(e). We believe these proposed minimum security standards for Tier 1 select agents would serve to further mitigate the potential for deliberate misuse of these select agents and toxins that could result in mass casualties or devastating effects to the economy, critical infrastructure, or public confidence.

These proposed changes are based on established security industry standards with respect to securing high risk material and developed in accordance with the experience and expertise of the Federal Select Agent Program and in consultation with DOD, FBI, and DHS security experts. They are necessary in order to further ensure the safety and security of those select agents and toxins that are proposed to be deemed Tier 1 agents. The requirements for working with all other select agents and toxins would remain unchanged with the exception of certain miscellaneous changes that are detailed below.

Security of Variola Major Virus and Variola Minor Virus

In recognition of the special public health risks associated with Variola major virus and Variola minor virus, we are also proposing to require additional physical security measures over and above those proposed for Tier 1. These additional requirements would be added as section 73.11(e)(5) (Security). We believe this change is necessary because Variola major virus and Variola minor virus were determined to pose a significantly higher public health risk than the other agents and toxins that were proposed for the Tier 1 select agents and toxins list. We also believe that it would not be appropriate to require that the special security procedures appropriate for Variola major virus and Variola minor virus be made applicable to other agents or toxins on a Tier 1 list.

Select Agent Inventory

Many commenters to the July 21, 2010 ANPRM pointed out that the requirement to account for individual vials of each pathogen is inappropriate for replicating biological agents. Commenters stated that this is a costly and burdensome responsibility for laboratories and their staff and that this requirement should be abolished except for Tier 1 agents.

We are not proposing any changes to the select agent regulations based on these comments. Currently, the select agent regulations state that an accurate, current inventory for each select agent (including viral genetic elements, recombinant nucleic acids, and recombinant organisms) held in long-term storage (placement in a system designed to ensure viability for future use, such as in a freezer or lyophilized materials) must be maintained. The requirement to account for individual vials of each pathogen in long term storage is necessary to ensure the biosecurity of select agents and toxins. Further guidance on this requirement can be found at *http://www.selectagents.gov.*

Definitions

In order to improve the clarity of the HHS Select Agent Regulations, we are proposing to add the following definitions to 42 CFR 73.1, to clarify the terms related to the identification of a *Restricted person: Adjudicated as a mental defective, Alien, Crime punishable by imprisonment for a term exceeding 1 year, Committed to any mental institution, Controlled substance, Indictment, Information security; Lawfully admitted for permanent residence, Mental institution,* and *Unlawful user of any controlled substance.* We believe that these definitions will assist Responsible Officials as well as those seeking approval to access select agents and toxins to better understand what status or activities, past or present, might prohibit such access.

Although these terms were undefined in the Bioterrorism Response Act, it is evident that Congress modeled many of them after the disqualifiers that are used by the Bureau of Alcohol, Tobacco, Firearms, and Explosives (ATF) when enforcing the Gun Control Act of 1968. Because the purpose of the Select Agent Program differs from ATF's enforcement actions under the Gun Control Act, we do not believe that these terms must be defined exactly the same. The Gun Control Act regulates access to firearms, while the Bioterrorism Response Act regulates access to biological agents and toxins that the government has recognized as having the potential to be used as weapons of mass destruction by the wrong hands.

Nevertheless, we looked at the statutory and regulatory definitions of these terms under the Gun Control Act when drafting our definitions. With the exception of the term ''crime punishable by imprisonment for a term exceeding 1 year,'' we decided to adopt the applicable definitions used by ATF.

We are proposing to define a ''crime punishable by imprisonment for a term exceeding 1 year'' as ''any Federal, State, or foreign offense for which the maximum penalty, whether or not imposed, is capital punishment or imprisonment in excess of 1 year. What constitutes a conviction of such a crime shall be determined in accordance with the law of the jurisdiction in which the proceedings were held. Any conviction that has been set aside or nullified as a matter of law or for which a person has been pardoned shall not be considered a conviction for purposes of this part.'' Contrary to definition of this term used under the Gun Control Act, we have decided that foreign offenses should be considered a disqualifier. In doing so we are aware of the Supreme Court's decision in *Small* v. *United States,* 544 U.S. 385 (2005) in which the court, interpreting the provisions of 18 U.S.C. 922(g)(1), held that phrase ''convicted in any court'' refers only to U.S. courts, not to foreign courts. In its opinion interpreting the Gun Control Act, the court stated that ''the statute itself and its history offer only congressional silence'' as to whether Congress considered whether the statutory

language included foreign convictions. In the case of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (Bioterrorism and Response Act), we believe Congress spoke clearly about their desire to limit or deny access to select agents and toxins for those who have committed serious crimes regardless of where committed.

We believe that in light of the threat of bioterrorism attacks, Congress would not want to exclude an individual convicted of a U.S. offense from having access to BSAT, but still allow access to an individual convicted in a foreign court of a similar offense.

As a part of the safeguard and security section of the Bioterrorism Response Act, Congress not only put select agents and toxins off limits to a ''restricted person,'' as that term is defined by 18 U.S.C. 175b, but to those who are ''reasonably suspected by any Federal law enforcement or intelligence agency of'' (1) committing a ''Federal crime of terrorism'' transcending national boundaries (18 U.S.C. 2332b), (2) the knowing involvement with an organization that engages in domestic or international terrorism or with any other organization that engages in international crimes of violence; or (3) being an agent of a foreign power. We believe it would be an inconsistent reading of statutory authority to allow the Secretary to limit or deny access to select agents and toxins to someone identified by the Attorney General as being reasonably suspected of committing a Federal crime of terrorism transcending national boundaries but to be powerless in cases where a person had actually been convicted of a serious crime in a foreign country. We also believe that the instances of regulation can be distinguished in that with regard to the Gun Control Act of 1968, the government is regulating access to guns while with respect to the Bioterrorism Response Act, the government is regulating access to biological agents and toxins that the government has recognized as having the potential to be used in the wrong hands as weapons of mass destruction.

We specifically request comments on the use of a foreign conviction as a predicate for denying access to select agents and toxins. We recognize that there can be significant differences between foreign convictions and domestic convictions. For example, foreign legal systems may not provide the same due process safeguards afforded to citizens of the United States, including impartial tribunals and jury trials. Additionally, foreign countries may punish conduct that is permitted under domestic law or may require more severe penalties than under domestic law. We note that in the past, courts have applied the criteria set forth in Section 482 of the Restatement (third) of Foreign Relations Law of the United States (1986) in determining whether a foreign judgment should be recognized in the United States. That Section provides that a court in the United States may not recognize a judgment of the court of a foreign state if the judgment was rendered under a judicial system that does not provide impartial tribunals or procedures compatible with due process of law or the court that rendered the judgment did not have jurisdiction over the defendant in accordance with the law of the rendering state. It further provides that a court in the United States need not recognize a judgment of the court of a foreign state if the court that rendered the judgment did not have jurisdiction of the subject matter of the action, the defendant did not receive notice of the proceedings in sufficient time to enable him to defend, the judgment was obtained by fraud, the cause of action on which the judgment was based, or the judgment itself, is repugnant to the public policy of the United States or of the State where recognition is sought, the judgment conflicts with another final judgment that is entitled to recognition, or the proceeding in the foreign court was contrary to an agreement between the parties to submit the controversy on which the judgment is based to another forum. We are seeking comment on whether these criteria should be applied in considering whether access to select agents and toxins should be denied based on a foreign conviction or whether other criteria or factors would be appropriate to consider.

Also, contrary to the definition used by ATF, we are proposing that a state offense classified by the laws of that state as a misdemeanor, but which has a term of imprisonment exceeding one year, should be considered a disqualifier—even though an individual convicted of the same offense would not be disqualified under the Gun Control Act. Finally, we are proposing to permit access to BSAT to individuals who have been convicted of a disqualifying offense if their convictions have been set aside or nullified as a matter of law or they have been pardoned. Although such language was not specifically included in the Bioterrorism Response Act, we believe that we should take into account certain post-conviction actions when determining whether we should deny an individual access to BSAT.

We are proposing to add a definition for *Occupational exposure* based on the definition used in the Occupational Safety and Health Administration (OSHA) regulations found in 29 CFR 1910.1030. In addition, we are proposing to add the definitions for *Recombinant and Synthetic Nucleic Acids* to clarify the existing regulations, as the term ''recombinant nucleic acids'' is employed but not defined, and synthetic nucleic acids are not currently addressed in the HHS Select Agent Regulations.

Recombinant/Synthetic Nucleic Acids

In addition to adding the proposed definition for *Recombinant and Synthetic Nucleic Acids,* we are also proposing to add the phrase ''and/or synthetic'' after the word ''Recombinant'' throughout 73.3 (c) and 73.4 (c). Current regulations regarding recombinant nucleic acids and recombinant organisms focus solely on the use of recombinant technology in the generation of these genetic elements. Since synthetic DNA technology may also be used to generate such genetic elements, we are proposing to expand the category of genetic elements to include recombinant and/or synthetic DNA.

Toxins

Sections in §§ 73.3 and 73.4 of 42 CFR contain provisions for toxins regulated by HHS under part 73. In 42 CFR 73.3(e) and 73.4(e), we are proposing to clarify that the ''inactive form of a select toxin'' may be excluded from regulation since the current term, ''attenuated strain of toxin'' is scientifically inaccurate. ''Attenuated'' is a term that is applied to living organisms and toxins are not living organisms. Since ''Inactive form of a select toxin'' is a more accurate term, we are proposing to amend the regulations to include the correct terminology.

Section 42 CFR 73.3(d)(3) specifies the permissible select toxin amounts under the control of a principal investigator, treating physician or veterinarian, or commercial manufacturer or distributor that are excluded from the requirements of the select agent regulations. We are proposing to require that the person transferring toxins in amounts which would otherwise be excluded from the provisions of the select agent regulations would be excluded only if the transferor: (1) Can show that the transferor used due diligence (i.e., reasonably justified by a prophylactic, protective, bona fide research, or other peaceful purpose) to assure that the recipient has a legitimate need to handle

or use such toxins; and (2) reports to CDC if they detect a known or suspected violation of Federal law or become aware of suspicious activity related to the toxin. The HHS Secretary would also retain the authority to, without prior notification, inspect and copy or request the submission of the due diligence documentation. It should be noted that this proposed requirement would not apply to toxins exempted under Section 42 CFR 73.5(c).

We are proposing to add 42 CFR 73.3(d)(4) which would state, ''Notwithstanding section (i) above, an animal inoculated with or exposed to an HHS select toxin.'' The current regulations consider that an animal injected with or exposed to (e.g., by inhalation, dermal absorption, or ingestion) a select toxin is a ''select toxin'' itself and would need to be housed in a registered space. This change would allow animals injected with or exposed to a select toxin to not be considered a ''select toxin.'' Therefore, the animals would not need to be housed in a registered space. This change will eliminate an unnecessary burden on a registered entity because recovering the toxin from within an animal subject is highly difficult and such removal is unlikely to produce a reasonable yield of recovery. In addition, there is uncertainty as to whether the toxin would remain active when recovered from the animal. For these reasons, it is highly unlikely that once introduced into an animal, sufficient toxin would be able to be recovered to pose a significant hazard to public health.

Exemptions

The regulations found in 42 CFR 73.5 and 73.6 requires identified select agents listed on the CDC's Category A Bioterrorism Agents list (i.e., agents that pose a risk to national security because they can be easily disseminated or transmitted from person to person; result in high mortality rates and have the potential for major public health impact; might cause public panic and social disruption; and require special action for public health preparedness) contained in a specimen presented for diagnosis or verification to be immediately reported to APHIS or CDC by telephone, facsimile, or e-mail.

We are proposing to amend this immediate notification to only those select agents and toxins identified as Tier 1 agents because these agents and toxins present the greatest risk of deliberate misuse with the most significant potential for mass casualties.

Responsible Official

The regulations found in 42 CFR 73.9 set out requirements for entities requesting to work with select agents and toxins to designate a Responsible Official, who ensures that the entity meets the requirements of the regulations.

We are proposing to add a specific requirement that all Responsible Officials possess the appropriate training or expertise to execute their required duties. We are also proposing to add a requirement that the Responsible Official's regular place of employment or principal duty station must be collocated in close proximity with the physical location of the registered entity entered in section 1A of APHIS/CDC Form 1 (Application for Registration for Possession, Use, and Transfer of Select Agents and Toxins OMB Control No. 0579–0213, OMB Control No. 0920–0576, Expiration Date 12/31/2011). We believe that the Responsible Official should have a physical (and not merely a telephonic or audio/visual) presence at the entity to ensure that the entity is in compliance with the select agent regulations and be able to quickly respond to on-site incidents involving select agents and toxins.

We are also proposing to clarify the role of Alternate Responsible Official in order to definitively establish that the Alternate Responsible Official must have the knowledge and authority to act for the Responsible Official in his/her absence.

Access to Select Agents and Toxins

We are proposing to amend the regulations in 42 CFR 73.10. These regulations establish parameters for restricting access to select agents and toxins and the process by which individuals may be approved by HHS/CDC or USDA/APHIS for access to select agents and toxins after the completion of a security risk assessment by the Attorney General. Specifically, we are proposing to add new provisions by which individuals may have access to select agents and toxins at entities other than the individual's ''home'' entity.

We are also proposing to decrease the maximum length of time in which a security risk assessment will be valid from five years to three years in order to more expeditiously identify individuals who may have fallen into one of the prohibited or restricted categories.

Security Plan

The regulations in 42 CFR 73.11 establish the requirements for developing and implementing a security plan sufficient to safeguard select agents or toxins against unauthorized access, theft, loss, or release. The regulations currently require that the security plan must be submitted by all regulated entities upon request. We are proposing to amend § 73.11 to require that the security plan be submitted for initial registration and renewals of registration.

Since we believe animals and plants exposed to or infected with a select agent should be handled as a select agent and safeguarded in the same manner as a select agent, we are proposing to require that the security plan include provisions to address safeguarding of animals or plants intentionally or exposed to or infected with select agents against unauthorized access, theft, loss or release. We are not requiring this plan to address procedures concerning animals exposed to toxins because, as discussed above, it is highly unlikely that once introduced into an animal, sufficient toxin can be recovered to pose a significant hazard to public health and safety. We are additionally proposing to add a requirement that the security plan include procedures for the Responsible Official to immediately notify the Federal Bureau of Investigation (FBI) of suspicious activity that may be criminal in nature and related to the entity, its personnel, or its select agents or toxins. We believe that any criminal activity of this kind should be immediately and directly reported to the FBI so they can initiate an investigation or other appropriate response.

We are proposing that the security plans of entities with select agents and toxins must include provisions for information security. These information security provisions would include network connectivity monitoring, restriction of user permissions so that only mission-specific files and applications may be accessed, measures to prevent network infiltration by malicious code, configuration management including regular patching and system and software updates, and backup security measures in the event that access control systems and/or surveillance devices are rendered inoperable. We believe that information security enhancements are important because the security of records or information systems that could allow an individual to gain access to the select agents or toxins should be safeguarded to prevent unauthorized access, theft, loss, or release of these materials.

We are proposing to codify current practices for shipping, receiving, and storage of select agents and toxins to ensure that the entity has documented

processes for securing and monitoring the shipment, receipt, and storage of these items. These changes would serve to decrease the chance that such materials would be made available to an unauthorized individual or an individual without a legitimate use for the material.

We are also proposing to remove the reference in 73.11(e), ''Laboratory Security and Emergency Response Guidance for Laboratories Working with Select Agents'' in Morbidity and Mortality Weekly Report (December 6, 2002) because we posted a security information guidance document in March 2007 that supersedes this reference.

Biosafety Plan

We are proposing to amend the regulations in 42 CFR 73.12 to require that a regulated entity's biosafety plan address procedures concerning animals or plants accidentally or intentionally exposed to or infected with a select agent. We are not requiring this plan to address procedures concerning animals exposed to toxins. As stated previously, this is because it is highly unlikely that once introduced into an animal, sufficient toxin can be recovered to pose a significant hazard to public health, agriculture or agriculture products.

We are also proposing that the biosafety plan must include provisions for the implementation of an occupational health program for individuals with access to Tier 1 select agents and toxins. We believe aspects of an individual's health may be relevant to their suitability to access biological select agents and toxins; identification of potential health problems and review of medication or treatment that may affect security and safety is paramount; and, occupational health programs should inform scientists of the types of medications and treatments that might have a potential deleterious effect on working safely and securely with select agents and toxins.

Restricted Experiments

The regulations in 42 CFR 73.13 concern restricted experiments that may not be performed unless approved by the HHS Secretary. We are proposing to add language in order to expand the current ''restricted experiment'' approval requirement to include all experiments involving the creation of drug resistant select agents that are not known to acquire the resistance naturally, if such acquisition could compromise the use of the drug to control disease agents in humans, veterinary medicine, or agriculture and not just those involving recombinant DNA. The regulations in 42 CFR 73.13 concern restricted experiments which may not be performed unless approved by the HHS Secretary. Furthermore, we are proposing to state that, in addition to the existing prohibition on conducting restricted experiments without express approval, entities may not possess the products (i.e., creation of drug resistant select agents that are not known to acquire the resistance naturally, if such acquisition could compromise the use of the drug to control disease agents in humans, veterinary medicine, or agriculture, or recombinant and or synthetic DNA containing genes for the biosynthesis of select toxins lethal for vertebrates at an LD[50] < 100 ng/kg body weight resulting from restricted experiments) resulting from restricted experiments without the express approval of the HHS Secretary. We are also proposing to remove recombinant technology as the only determining factor for a restricted experiment. Current regulations regarding restricted experiments focus solely on the use of recombinant technology in the generation of drug resistant select agents or biosynthesis of toxins lethal to vertebrates. Since synthetic DNA technology or selection in sublethal exposures may also be used to generate such products, we are proposing to expand the category of restricted experiments to include passive selection, recombinant and/or synthetic DNA.

Incident Response

The regulations in 42 CFR 73.14 contain requirements for development of incident response plans. We are proposing to specify that each entity's incident response plan be based upon a site-specific risk assessment. We believe this change would further ensure the specificity and quality of the plan. In addition, we are proposing that the incident response procedures contain specific provisions concerning animals or plants accidentally or intentionally exposed to or infected with a select agent. We are not requiring this plan to address procedures concerning animals exposed to toxins. As stated previously, this is because it is highly unlikely that once introduced into an animal, sufficient toxin can be recovered to pose a significant hazard to public health, agriculture or agriculture products.

Training

We are proposing to amend the regulations in 42 CFR 73.15 that contain provisions of mandatory training for staff and visitors who work in or visit areas where select agents or toxins are handled or stored to provide security awareness and incident response training. We believe these additional training initiatives are needed to ensure that (1) personnel will be better trained to safeguard select agents and toxins from thefts, losses, intentional releases, or unauthorized access and (2) personnel will be better trained to ensure that select agents and toxins are safeguarded during exigent circumstances that include natural and man-made disasters. We are also proposing to clarify the language regarding the level of training that staff and visitors would be required to receive in order to establish that training for escorted personnel based on the risk associated with accessing areas where select agents and toxins are used and/or stored. Currently, refresher training is required to be provided once a year. We are proposing to require that such training also be provided if a registered entity's security, incident response, or biosafety plans are substantively altered. Finally, we are proposing to specify that the Responsible Official ensure maintenance of training records. Currently, there is no particular person designated as the entity's required record keeper, only that a training record must be kept.

Transfers

The transportation in commerce of hazardous materials, including select agents and toxins, is governed by the United States Department of Transportation's Hazardous Material Regulations found in Title 49 of the Code of Federal Regulations, parts 100–185. The regulations in 42 CFR 73.16 do not impose requirements on the transportation in commerce of select agents or toxins. We are proposing to clarify when ''transportation in commerce'' begins and ends to better allow registered individuals and entities to adequately address those situations when a select agent or toxin is (1) ready to be packaged for transportation, (2) packaged for shipment, or (3) received and handled by a person with approval to access select agents and toxins. In addition, we are proposing language to codify policies and practices into a standard for shipping, receiving, and storage of select agents and toxins to ensure that the entity has documented processes for securing and monitoring the shipment, receipt, and storage of select agents and toxins that make it extremely unlikely that such materials would be made available to an unauthorized individual or an individual without a legitimate use for the material. We note the concerns identified in two HHS Office of Inspector General (OIG) audits regarding

vulnerabilities that may occur during the shipment of select agents and toxins. HHS/CDC reviewed how entities ship select agents and toxins and evaluated ways to improve this process to ensure they are not only safeguarded against unauthorized access, but also against theft, loss, or release. We believe that the proposed amendments will help address OIG's concerns.

Records

The regulations in 42 CFR 73.17 address recordkeeping requirements for regulated entities as those records that relate to select agents and toxins. We are proposing to clarify the current language that an accurate, current inventory needs to be maintained for each select agent that the entity possesses including synthetic select agent organisms and any animals or plants intentionally or unintentionally exposed to or infected with a select agent (including number and species, location and appropriate disposition). We believe this clarification is needed to ensure that accurate, current records are maintained for all select agents that the entity possesses. We are currently soliciting comments from the public (as well as affected agencies) concerning our proposed information collection and recordkeeping requirements. Please send written comments to Daniel Holcomb, CDC Acting Reports Clearance Officer, 1600 Clifton Road, MS–D74, Atlanta, GA 30333 or send an e-mail to *omb@cdc.gov*. Please state that your comments refer to Possession, Use, and Transfer of Select Agents and Toxins (OMB Control No. 0920–0576).

As previously stated, we are not proposing to require regulated entities to keep records regarding animals exposed to toxins because it is highly unlikely that once introduced into an animal, sufficient toxin can be recovered to pose a significant hazard to public health, agriculture or agriculture products.

Administrative Review

We are proposing to amend the regulations in 42 CFR 73.20 that addresses the administrative review of an individual or entity's denial, revocation, or suspension of registration and access approval. Specifically, we are proposing to modify the current regulations in order to allow individuals more time to gather the necessary components of their appeal following the denial, limitation, or revocation of access approval. Currently, this process must be initiated in 30 calendar days. We are proposing to extend the deadline to 180 calendar days. We believe this change would provide individuals with sufficient time to gather all documents necessary to support an appeal. Finally, we are proposing to remove the provision ''Where the denial, revocation, or suspension of an individual's access approval is based upon identification by the Attorney General, the request for review will be forwarded to the Attorney General'' to provide clarification that the decision regarding the appeal is determined by the HHS Secretary.

Guidance Documents

We are specifically requesting comments from the regulated community and any other interested persons on the development of one or more guidance documents that would serve to provide assistance in the interpretation of the select agent regulations.

The areas where guidance documents may be developed in relation to the select agent regulations include, but are not limited to:

1. Aspects of the required security plan. These may include, but are not limited to:

- Standards for information security;
- Development of suitability or personnel reliability practices, including pre-access and ongoing assessment processes of persons who will have access to Tier 1 select agents or toxins;
- Procedures for the method by which an entity's Responsible Official will coordinate his or her efforts with the entity's safety and security professionals to ensure security of Tier 1 select agents or toxins and have access to relevant information from all professionals dealing with biological select agents and toxins safety and security;
- Development of a self- and peer-reporting program to track incidents or conditions that could affect an individual's ability to safely access or work with Tier 1 select agents and toxins; and
- Layered physical security protection of assets for entities housing Tier 1 select agents and toxins.

2. Aspects of the required biosafety plan, e.g., components of an occupational health program for individuals with access to Tier 1 select agents and toxins; and

3. Aspects of the required training, e.g., best practices for development of a security awareness training program.

We welcome public comment on the use of Web sites, articles, or other sources that may be used to develop such documents, in addition to suggestions as to what elements should be included as useful examples. These documents would serve as a resource to the regulated community as a whole.

III. Required Regulatory Analyses

a. Executive Orders 12866 and 13563

Executive Orders 12866 and 13563 direct agencies to assess all costs and benefits of available regulatory alternatives and, if regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety effects, distributive impacts, and equity). E.O. 13563 emphasizes the importance of quantifying both costs and benefits, of reducing costs, of harmonizing rules, and of promoting flexibility.

Under E.O. 12866 HHS must determine whether a regulatory action is ''significant.'' A ''significant regulatory action'' under E.O. 12866 is defined as (1) an action that is likely to result in a rule that may have an annual effect on the economy of $100 million or more, or adversely and materially affects a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or state, local or tribal governments or communities (or an economically significant action); (2) creates a serious inconsistency or otherwise interferes with an action taken or planned by another agency; (3) materially alters the budgetary impact of entitlements, grants, user fees or loan programs or the rights and obligations of recipients; or (4) raises novel legal or policy issues. Because this rulemaking proposes changes to how a subset of select agents and toxins are protected, this rule is has been determined to be ''significant'' under E.O. 12866 and, therefore, has been reviewed by the Office of Management and Budget (OMB).

We have prepared an economic analysis for this rule. The economic analysis provides a cost-benefit analysis, as required by E.O. 12866, and an initial regulatory flexibility analysis (See III.b.) that examines the potential economic effects of this proposed rule on small entities, as required by the Regulatory Flexibility Act. The economic analysis is summarized below. Copies of the full analysis are available by contacting the person listed under **FOR FURTHER INFORMATION CONTACT** or on the Federal Select Agent Program Web site at: *http://www.selectagents.gov/* or on the public docket at *http://www.regulations.gov.*

Summary of the Regulatory Impact Analysis

Certain pathogens or biological toxins that are released intentionally or accidentally can result in disease, wide-ranging and devastating impacts on the economy, disruption to society, diminished confidence in public and private institutions, and large-scale loss of life. People or livestock can be exposed to these agents from inhalation, through the skin, or by the ingestion of contaminated food, feed, or water. Similarly, crops can be exposed to biological pathogens in several ways—at the seed stage, in the field, or after harvest.

The *Public Health Security and Bioterrorism Preparedness and Response Act of 2002* (Pub. L. 107–188) (the Act) provides for the regulation of certain biological agents and toxins that have the potential to pose a severe threat to both human and animal health, to plant health, or to animal and plant products. APHIS and CDC have the primary responsibility for implementing the provisions of the Act within USDA and HHS, respectively. Within APHIS, Veterinary Services (VS) select agents and toxins are those that have been determined to have the potential to pose a severe threat to animal health or animal products, and Plant Protection and Quarantine (PPQ) select agents and toxins are those that have been determined to have the potential to pose a severe threat to plant health or plant products. HHS select agents and toxins are those that have been determined to have the potential to pose a severe threat to human health. APHIS and CDC coordinate regulatory activities for overlap select agents and toxins that have been determined to pose a severe threat to human and to animal health or animal products.

Sections 201 and 212(a)(2) of the Act requires a biennial review and republication of the select agent and toxin list, with revisions as appropriate in accordance with this law. See 42 U.S.C. 262a(a)(2) and 7 U.S.C. 8401(a)(2), respectively. This rule would implement the recommendations of the third biennial review of the list. Furthermore, revision of these regulations would incorporate the recommendations developed as a result of E.O. 13546, ''Optimizing the Security of Biological Select Agents and Toxins in the United States,'' which requires that the HHS and USDA Secretaries publish proposed regulations to establish risk-based tiering of the select agent list, and revise the regulations, rules, and guidance to accommodate a tiered select agent list no later than October 2011.

In addition, we are proposing several amendments to the regulations, including the addition of definitions and clarification of language concerning security, training, biosafety/biocontainment, and incident response. These changes would increase the applicability and effectiveness of the select agent regulations and provide for enhanced program oversight. This rule would update the USDA, HHS, and overlap select agent and toxin lists. The regulation of select agents and toxins is intended to prevent their misuse and thereby reduce the potential for those pathogens to harm humans, animals, animal products, plants or plant products in the United States. Should any select agent or toxin be intentionally or unintentionally released into the environment, the consequences would be significant. Consequences could include disruption of markets, difficulties in sustaining an adequate food and fiber supply, and the potential spread of disease infestations over large areas. The entities most likely to be affected by this rule would be those laboratories and other institutions conducting research and related activities that involve the use of the newly categorized Tier 1 select agents and toxins. The impact of the changes to the regulations is expected to be minimal. Based on information obtained through site-specific inspections, we believe that very few entities would incur significant costs for compliance. Many of the proposed changes to the regulations would impose an added time cost to measures already required for compliance, with respect to security, biocontainment/biosafety, and incident response plans, information security, and ongoing background checks. While the total cost of the proposed regulations is estimated to range between $4.9 million and $6.4 million, we believe many of these costs are currently incurred by affected entities as generally recognized practices. Costs actually incurred would depend upon the number of computers and facility systems that require the proposed enhanced security. The expected benefits of strengthened safeguards against the unintentional or deliberate release of a select agent or toxin exceed the estimated costs of the proposed measures. Based on the information we have, there is no reason to conclude that adoption of this proposed rule would result in any significant economic effect on a substantial number of small entities. The entities are those laboratories and other institutions conducting research and related activities entities in possession of Tier 1 select agents or toxins, and, to a somewhat lesser extent, those entities possessing the newly added select agents and toxins. The economic analysis presents categories and information from the Department of Commerce and the Small Business Administration for those entities we have identified as most likely to be affected by this rule. While we believe affected entities are contained within these categories, we are seeking further information regarding how many entities fall specifically into each category, and are therefore, inviting comments on potential effects. In particular, we are interested in determining the number and kind of small entities that may incur benefits or costs from the implementation of this proposed rule.

This proposed rule would update the APHIS, CDC, and overlap select agent and toxin lists. The regulation of select agents and toxins is intended to prevent their misuse and thereby reduce the potential for those pathogens to harm humans, animals, animal products, plants or plant products in the United States. Should any select agent or toxin be intentionally or unintentionally released into the environment, the consequences would be significant. Consequences could include disruption of markets, difficulties in sustaining an adequate food and fiber supply, and the potential spread of disease infestations over large areas. The entities most likely to be affected by this rule would be those laboratories and other institutions conducting research and related activities that involve the use of the newly categorized Tier 1 select agents and toxins. The impact of the changes to the regulations is expected to be minimal, however. Based on information obtained through site-specific inspections, indications are that very few entities would incur significant costs for compliance. Many of the proposed changes to the regulations would impose an added cost of the time spent on documenting measures already required for compliance, with respect to security, biocontainment/biosafety, and incident response plans, information security, and ongoing background checks. While the total costs imposed by the proposed regulations are estimated to range between $5.30 million and $6.95 million, including costs to government, we believe many of these costs are incurred through observance of generally recognized industry standards. Costs actually incurred would depend upon the extent to which current facility

practices will need to be enhanced based on the proposed requirements. The expected benefits of strengthened safeguards against the costs associated with unintentional or deliberate release of select agents or toxins would greatly exceed the estimated costs of the proposed measures. The cost associated with a single outbreak have been known to exceed $100 million as outlined in the Regulatory Impact Analysis. Deliberate introduction greatly increases the probability of a select agent or toxin becoming established and causing wide-ranging and devastating impacts on an economy, loss of market access for consumer goods and services, disruption to society, and diminished confidence in public and private institutions.

This analysis reviews expected benefits and costs of the proposed rule in accordance with Executive Orders 12866 and 13563. Possible impacts for small entities are also considered as required by the Regulatory Flexibility Act, which requires agencies to prepare and make available for public comment an initial regulatory flexibility analysis that describes expected impacts of a proposed rule on small businesses, small organizations and small governmental jurisdictions.

Based on the information we have, there is no reason to conclude that adoption of this proposed rule would result in any significant economic effect on a substantial number of small entities. However, we do not currently have all of the data necessary for a comprehensive analysis of the effects of this proposed rule on small entities. Therefore, we are inviting comments on potential effects. In particular, we are interested in determining the number and kind of small entities that may incur benefits or costs from the implementation of this proposed rule.

b. Regulatory Flexibility Act

The Regulatory Flexibility Act (RFA) (5 U.S.C. 601 *et seq.*) requires an agency to consider the potential impact of its regulations on small entities, including small businesses, small governmental units, and small not-for-profit organizations. We certify that this rule will not have a significant economic impact on a substantial number of small entities within the meaning of the RFA. Therefore, a regulatory flexibility analysis as provided for under the RFA is not required.

c. Paperwork Reduction Act of 1995

In accordance with section 3507(d) of the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 *et seq.*), the information collection or recordkeeping requirements included in this proposed rule have been submitted for approval to the Office of Management and Budget (OMB). Please send written comments to the Office of Information and Regulatory Affairs, OMB, Attention: Desk Officer for APHIS, Washington, DC 20503. Please state that your comments refer to Docket Nos. APHIS–2009–0070 and CDC–2011–0012. Please send a copy of your comments to: (1) Docket Nos. APHIS–APHIS–2009–0070 and CDC–2011–0012, Regulatory Analysis and Development, PPD, APHIS, Station 3A–03.8, 4700 River Road Unit 118, Riverdale, MD 20737–1238, and (2) Clearance Officer, OCIO, USDA, room 404–W, 14th Street and Independence Avenue, SW., Washington, DC 20250. A comment to OMB is best assured of having its full effect if OMB receives it within 30 days of publication of this proposed rule.

The Bioterrorism Preparedness Act is designed to prevent, prepare for and respond to bioterrorism and other public health emergencies. The law requires individuals possessing agents or toxins deemed a severe threat to human, animal, or plant health, or to animal or plant products, to be registered with the Secretary of Agriculture or the Secretary of Health and Human Services, unless they have been specifically exempted.

This proposed rule entails the use of a number of separate forms designed to obtain critical information concerning individuals or entities in possession of certain agents or toxins, as well as the specific characteristics of the agents or toxins—including name, strain, and genetic information. This data is needed, in part, to allow APHIS and CDC to determine the biosafety level of an entity as well as the entity's biosecurity situation. This, in turn, helps APHIS and CDC ensure that appropriate safeguard, containment, and disposal requirements commensurate with the risk of the agent or toxin are present at the entity, thus preventing access to such agents and toxins for use in domestic or international terrorism. Facilities containing select agents will be required to maintain records on animals and plants, and revise their Biosafety/Biocontainment Plan and Incident Response Plan for review by APHIS and CDC upon request.

Information to determine that individuals seeking to register have a lawful purpose to possess, use, or transfer agents or toxins will also be requested as part of the registration process. In addition, we will be requesting submission of their Security Plan for our review.

APHIS and CDC are asking OMB to approve, for 3 years, the use of these information collections, associated with its efforts to more closely regulate select agents or toxins that could be used to commit acts of domestic or international terrorism. We are soliciting comments from the public (as well as affected agencies) concerning this information collection activity. APHIS and CDC need this outside input to help accomplish the following:

(1) Evaluate whether the proposed information collection is necessary for the proper performance of our agency's functions, including whether the information will have practical utility;

(2) Evaluate the accuracy of our estimate of the burden of the proposed information collection, including the validity of the methodology and assumptions used;

(3) Enhance the quality, utility, and clarity of the information to be collected; and

(4) Minimize the burden of the information collection on those who are to respond (such as through the use of appropriate automated, electronic, mechanical, or other technological collection techniques or other forms of information technology; e.g., permitting electronic submission of responses).

Estimate of burden: Public reporting burden for this collection of information is estimated to average 2.3187883 hours per response.

Respondents: Researchers, universities, research and development organizations, commercial manufacturers, non-profit institutions, diagnostic laboratories and other interested parties who possess, use, or transfer agents or toxins deemed a severe threat to human, animal or plant health, or to animal or plant products.

Estimated annual number of respondents: 386.

Estimated annual number of responses per respondent: 12.230569.

Estimated annual number of responses: 4,721.

Estimated total annual burden on respondents: 10,947 hours. (Due to averaging, the total annual burden hours may not equal the product of the annual number of responses multiplied by the reporting burden per response.)

Section	Form name	Number of respondents	Number of responses per respondent	Average burden per response (in hours)	Total burden hours
9 CFR 121.5 and 6, 7 CFR 331.5, 43 CFR 73.5 and 6.	Report of Identification of a Select Agent or Toxin.	161	3	1	299
§ 121.7, § 331.7, § 73.7	Application for Registration	7	1	5	35
§ 121.7, § 331.7, § 73.7	Amendment to a Certificate of Registration.	380	7	1	1,955
§ 121.11, § 331.11, § 73.11	Security Plan	380	1	5	1,900
§ 121.12, § 331.12, § 73.12	Biosafety/Biocontainment Plan	380	1	8	3,040
§ 121.13, § 331.13, § 73.13	Request Regarding a Restricted Experiment.	160	1	2	320
§ 121.14, § 331.14, § 73.14	Incident Response Plan	380	1	5	1,900
§ 121.15, § 331.15, § 73.15	Training	380	1	1	380
§ 121.16, § 331.16, § 73.16	Request to Transfer Select Agents and Toxins.	290	1	2	580
§ 121.17, § 331.17, § 73.17	Records	295	1	0.5	148
§ 121.19, § 331.19, § 73.19	Notification of Theft, Loss, or Release.	195	1	2	390

Copies of this information collection can be obtained from Mrs. Celeste Sickles, APHIS' Information Collection Coordinator, at (301) 851–2908.

d. Executive Order 12988: Civil Justice Reform

This proposed rule has been reviewed under E.O. 12988, Civil Justice Reform. If this proposed rule is adopted: (1) All State and local laws and regulations that are inconsistent with this rule will be preempted; (2) no retroactive effect will be given to this rule; and (3) administrative proceedings will not be required before parties may file suit in court challenging this rule.

e. Executive Order 13132: Federalism

This rule has been reviewed under E.O. 13132, Federalism. The rule does not impose any regulation that would preempt State, local, and Indian Tribe requirements, or that would have any substantial direct effects on the States, or on the distribution of power and responsibilities among the various levels of government.

f. Plain Writing Act of 2010

Under Public Law 111–274 (October 24, 2010), executive branch Departments and Agencies are required to use plain language in documents that explain to the public how to comply with a requirement the Federal Government administers or enforces. HHS has attempted to use plain language in promulgating the proposed rule consistent with the Federal Plain Writing Act guidelines.

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List of Subjects in 42 CFR Part 73

Biologics, Incorporation by reference, Packaging and containers, Penalties, Reporting and recordkeeping requirements, Transportation.

For the reasons stated in the preamble, the Centers for Disease Control and Prevention, United States Department of Health and Human Services, proposes to amend 42 CFR part 73 as follows:

PART 73—SELECT AGENTS AND TOXINS

1. The authority citation for part 73 continues to read as follows:

Authority: 42 U.S.C. 262a; sections 201–204, 221 and 231 of Title II of Public Law 107–188, 116 Stat 637 (42 U.S.C. 262a).

2. Section 73.1 is amended by adding, in alphabetical order, definitions of *Adjudicated as a mental defective, Alien, Committed to any mental institution, Controlled substance, Crime punishable by imprisonment for a term exceeding 1 year, Indictment, Information security, Lawfully admitted for permanent residence, Mental institution, Occupational exposure, Recombinant and synthetic nucleic acids, Restricted person,* and *Unlawful user of any controlled substance* to read as set forth below.

§ 73.1 Definitions.

* * * * *

Adjudicated as a mental defective. A determination by a court, board, commission, or other lawful authority that a person, as a result of marked subnormal intelligence, or mental illness, incompetency, condition, or disease is a danger to himself/herself or to others or lacks the mental capacity to contract or manage his/her own affairs. The term includes a finding of insanity by a court in a criminal case and those persons found incompetent to stand trial or found not guilty by reason of lack of mental responsibility pursuant to articles 50a and 72b of the Uniform Code of Military Justice, 10 U.S.C. 850a, 876b.

Alien. Any person not a citizen or national of the United States.

* * * * *

Committed to any mental institution. A formal commitment of a person to any mental institution by a court, board, commission, or other lawful authority. The term includes a commitment to a mental institution involuntarily. The term includes commitment for mental defectiveness or mental illness. It also includes commitments for other reasons, such as for drug use. The term does not include a person in a mental institution for observation or a voluntary admission to a mental institution.

Controlled substance. A drug or other substance, or immediate precursor, as defined in section 102 of the Controlled Substances Act, 21 U.S.C. 802. The term includes, but is not limited to, marijuana and scheduled depressants, stimulants, and narcotic drugs. The term does not include distilled spirits, wine, malt beverages, or tobacco, as those terms are defined or used in Subtitle E of the Internal Revenue Code of 1986, as amended.

Crime punishable by imprisonment for a term exceeding 1 year. Any Federal, State, or foreign offense for which the maximum penalty, whether or not imposed, is capital punishment or imprisonment in excess of 1 year. What constitutes a conviction of such a crime shall be determined in accordance with the law of the jurisdiction in which the proceedings were held. Any conviction that has been set aside or nullified as a matter of law or for which a person has been pardoned shall not be considered a conviction for purposes of this part.

* * * * *

Indictment. A formal written accusation originating with a prosecutor and issued by a grand jury against a party charged with a crime. For the purpose of these regulations the term indictment includes any ''information'' that is a formal accusation of a crime, differing only in that it is being presented by a competent public officer on his oath of office, instead of a grand jury.

Information security. Protecting information and information systems from unauthorized access, use, disclosure, disruption, modification, or destruction in order to provide—

(1) *Integrity,* which means guarding against improper information modification or destruction, and includes ensuring information nonrepudiation and authenticity;

(2) *Confidentiality,* which means preserving authorized restrictions on access and disclosure, including means for protecting personal privacy and proprietary information; and

(3) *Availability,* which means ensuring timely and reliable access to and use of information.

* * * * *

Lawfully admitted for permanent residence. The status of having been lawfully accorded the privilege of residing permanently in the United States as an immigrant in accordance with the immigration laws, such status not having changed.

Mental institution. Includes mental health facilities, mental hospitals, sanitariums, psychiatric facilities, and other facilities that provide diagnoses by licensed professionals of mental retardation or mental illness, including a psychiatric ward in a general hospital.

* * * * *

Occupational exposure. Any reasonably anticipated skin, eye, mucous membrane, or parenteral contact with blood or other potentially infectious materials or toxins that may result from the performance of an employee's duties.

* * * * *

Recombinant and synthetic nucleic acids.

(1) Recombinant nucleic acid molecules that are constructed by joining nucleic acid molecules and that can replicate in a living cell;

(2) Synthetic nucleic acid molecules that are chemically, or by other means, synthesized or amplified nucleic acid molecules that may wholly or partially contain functional equivalents of nucleotides; or

(3) Molecules that result from the replication of those described in paragraphs (1) or (2) of this definition.

* * * * *

Restricted person. An individual who:

(1) Is under indictment for a crime punishable by imprisonment for a term exceeding 1 year;

(2) Has been convicted in any court of a crime punishable by imprisonment for a term exceeding 1 year;

(3) Is a fugitive from justice;

(4) Is an unlawful user of any controlled substance (as ''controlled substance'' is defined in section 102 of the Controlled Substances Act (21 U.S.C. 802));

(5) Is an alien illegally or unlawfully in the United States;

(6) Has been adjudicated as a mental defective or has been committed to any mental institution;

(7) 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 U.S.C. App. 2405(j)), section 620A of chapter 1 of part M of the Foreign Assistance Act of 1961 (22 U.S.C. 2371), or section 40(d) of chapter 3 of the Arms Export Control Act (22 U.S.C. 2780d), has made a determination (that remains in effect) that such country has repeatedly provided support for acts of international terrorism; or

(8) Has been discharged from the Armed Services of the United States under dishonorable conditions.

* * * * *

Unlawful user of any controlled substance. For purposes of this part, a person who uses a controlled substance and has lost the power of self-control with reference to the use of that controlled substance; and any person who is a current user of a controlled substance in a manner other than as prescribed by a licensed physician. Such use is not limited to the use of drugs on a particular day, or within a matter of days or weeks before, but rather that the unlawful use has occurred recently enough to indicate that the individual is actively engaged in such conduct. A person may be an unlawful current user of a controlled substance even though the substance is not being used at the precise time the person seeks to have access to a select agent or toxin. An inference of current use may be drawn from evidence of a recent use or possession of a controlled substance or a pattern of use or possession that reasonably covers the present time, e.g., a conviction for use or possession of a controlled substance within the past year; multiple arrests for such offenses within the past 5 years if the most recent arrest occurred within the past year, or persons found through a drug test to use a controlled substance unlawfully, provided that the test was administered within the past year. For a current or former member of the Armed Forces, an inference of current use may be drawn from recent disciplinary or other administrative action based on confirmed drug use, e.g., court-martial conviction, nonjudicial punishment, or an administrative discharge based on drug use or drug rehabilitation failure.

* * * * *

3. Section 73.3 is amended as follows:

a. By adding a sentence to the end of paragraph (a) to read as set forth below.

b. By revising paragraph (b) to read as set forth below.

c. In paragraph (c), in the introductory text, by adding the phrase ''and/or Synthetic'' after the word ''Recombinant'' each time it appears.

d. In paragraph (c)(2) introductory text, by adding the phrase ''and/or synthetic'' after the word ''Recombinant''.

e. By revising paragraph (d)(3) to read as set forth below.

f. By adding a new paragraph (d)(4) to read as set forth below.

g. By revising paragraph (e) to read as set forth below.

h. In paragraph (f)(3)(i), by removing the words ''Lassa fever virus, South American Haemorrhagic Fever virus (Junin, Machupo, Sabia, Flexal, Guanarito)'' and by adding the words ''Botulinum neurotoxin producing species of Clostridium.''

§ 73.3 HHS select agents and toxins.

(a) * * * The select agents and toxins marked with an asterisk (*) are designated as Tier 1 select agents and toxins and are subject to additional requirements as listed in this part.

(b) HHS select agents and toxins: [1]

Abrin
Botulinum neurotoxins*
Botulinum neurotoxin producing species of Clostridium*
Chapare
Clostridium perfringens epsilon toxin
Conotoxins
Coxiella burnetii
Crimean-Congo haemorrhagic fever virus
Diacetoxyscirpenol
Eastern Equine Encephalitis virus (North American genotypes)
Ebola virus*
*Francisella tularensis**
Lassa fever virus
Lujo
Marburg virus*
Monkeypox virus

Reconstructed replication competent forms of the 1918 pandemic influenza virus containing any portion of the coding regions of all eight gene segments (Reconstructed 1918 Influenza virus)

Ricin
Rickettsia prowazekii
Rickettsia rickettsii
Saxitoxin
Shiga-like ribosome inactivating proteins
Shigatoxin
South American Haemorrhagic Fever viruses
Guanarito
Junin
Machupo
Sabia
Staphylococcal enterotoxins (SE) A–E (SEA, SEB, SEC, SED, SEE)
T–2 toxin
Tetrodotoxin
Tick-borne encephalitis virus
Far Eastern subtype
Siberian subtype
Kyasanur Forest disease virus
Omsk hemorrhagic fever virus
Variola major virus (Smallpox virus)*
Variola minor virus (Alastrim)*
*Yersinia pestis**

* * * * *

(d) * * *

(3) Except as required in § 73.16(l), HHS toxins under the control of a principal investigator, treating physician or veterinarian, or commercial manufacturer or distributor, if:

(i) The aggregate amount does not, at any time, exceed the following amounts: 100 mg of Abrin; 0.5 mg of Botulinum neurotoxins; 100 mg of *Clostridium*

[1] Including all toxin derivatives, both naturally occurring and synthetic, that retain function.

perfringens epsilon toxin; 100 mg of Conotoxins; 1,000 mg of Diacetoxyscirpenol; 100 mg of Ricin; 100 mg of Saxitoxin; 100 mg of Shiga-like ribosome inactivating proteins; 100 mg of Shigatoxin; 5 mg of Staphylococcal enterotoxins; 1,000 mg of T–2 toxin; or 100 mg of Tetrodotoxin.

(ii) Amounts of toxins equal to or less than the amounts identified in paragraph (d)(3)(i) of this section are transferred only after the transferor uses due diligence and documents that the recipient has a legitimate need (i.e. reasonably justified by a prophylactic, protective, bona fide research, or other peaceful purpose) to handle or use such toxins. Notwithstanding the provisions of paragraph (d) of this section, the HHS Secretary retains the authority to, without prior notification, inspect and copy or request the submission of the due diligence documentation to the CDC.

(iii) The transfer of amounts of toxins equal to or less than the amounts identified in paragraph (d)(3)(i) of this section reports to CDC if they detect a known or suspected violation of Federal law or become aware of suspicious activity related to a toxin listed in section of this part.

(4) Notwithstanding paragraph (d)(3)(i) of this section, an animal inoculated with or exposed to an HHS select toxin.

(e) 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 that the attenuated strain or inactivated toxin does not pose a severe threat to public health and safety.

(1) To apply for exclusion, an individual or entity must submit a written request and supporting scientific information. A written decision granting or denying the request will be issued. An exclusion will be effective upon notification to the applicant. Exclusions will be listed on the National Select Agent Registry Web site at *http://www.selectagents.gov/.*

(2) If an excluded attenuated strain or inactivated toxin is subjected to any manipulation that restores or enhances its virulence or toxic activity, the resulting select agent or toxin will be subject to the requirements of this part.

* * * * *

4. Section 73.4 is amended as follows:

a. By adding a sentence to the end of paragraph (a) to read as set forth below.

b. By revising paragraph (b) to read as set forth below.

c. In paragraph (c), in the introductory text, by adding the phrase ''and/or synthetic'' after the word ''Recombinant'' each time it appears.

d. In paragraph (c)(2), by adding the phrase ''and/or synthetic'' after the word ''Recombinant''.

e. By revising paragraph (e) to read as set forth below.

f. In paragraph (f)(3)(i), by removing the words ''*Brucella melitensis,* Hendra virus, Nipah virus, Rift Valley fever virus, and Venezuelan equine encephalitis virus'' and adding the words ''*Burkholderia mallei* and *Burkholderia pseudomallei''* in their place.

§ 73.4 Overlap select agents and toxins.

(a) * * * The select agents and toxins marked with an asterisk (*) are designated as Tier 1 select agents and toxins and are subject to additional requirements as listed in this part.

(b) Overlap select agents and toxins:

*Bacillus anthracis;**
Brucella abortus;
Brucella melitensis;
Brucella suis;
*Burkholderia mallei;**
*Burkholderia pseudomallei;**
Hendra virus;
Nipah virus;
Rift Valley fever virus;
Venezuelan equine encephalitis virus: Epizootic Subtypes IAB, IC.

* * * * *

(e) 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.

(1) To apply for exclusion, an individual or entity must submit a written request and supporting scientific information. A written decision granting or denying the request will be issued. An exclusion will be effective upon notification to the applicant. Exclusions will be listed on the National Select Agent Registry Web site at *http://www.selectagents.gov/.*

(2) If an excluded attenuated strain or inactivated toxin is subjected to any manipulation that restores or enhances its virulence or toxic activity, the resulting select agent or toxin will be subject to the requirements of this part.

* * * * *

§ 73.5 [Amended]

5. Section 73.5(a)(3)(i) is amended by removing the words ''Lassa fever virus, South American Haemorrhagic Fever virus (Junin, Machupo, Sabia, Flexal, Guanarito)'' and by adding the words ''Botulinum neurotoxin producing species of *Clostridium''* in their place.

§ 73.6 [Amended]

6. Section 73.6(a)(3)(i) is amended by removing the words ''Brucella melitensis, Hendra virus, Nipah virus, Rift Valley fever virus, and Venezuelan equine encephalitis virus'' and adding the words ''*Burkholderia mallei* and *Burkholderia pseudomallei*'' in their place.

§ 73.8 [Amended]

7. Section 73.8 (a)(1) is amended by removing the words ''within any of the categories described in 18 U.S.C. 175b'' and adding the words ''a restricted person'' in their place.

* * * * *

8. Section 73.9 is amended as follows:

a. By redesignating paragraphs (a)(3) through (a)(5) as paragraphs (a)(4) through (a)(6) respectively.

b. By adding a new paragraph (a)(3) to read as set forth below.

c. In newly redesignated paragraph (a)(5), by removing the word ''and''.

d. By further redesignating newly redesignated paragraph (a)(6) as paragraph (a)(7).

e. By adding a new paragraph (a)(6) to read as set forth below.

f. By revising the first sentence of paragraph (b) to read as set forth below.

g. In paragraph (c)(1), by removing the words ''Bacillus anthracis, Botulinum neurotoxins, Brucella melitensis, Francisella tularensis, Ebola viruses, Hendra virus, Marburg virus, Lassa fever virus, Nipah virus, Rift Valley fever virus, South American Haemorrhagic Fever viruses (Junin, Machupo, Sabia, Flexal, Guanarito), Variola major virus (Smallpox virus), Variola minor (Alastrim), Venezuelan equine encephalitis virus and Yersina pestis'' and adding the words ''*Bacillus anthracis, Botulinum neurotoxins, Botulinum neurotoxin producing species of Clostridium, Burkholderia mallei, Burkholderia pseudomallei, Francisella tularensis, Ebola viruses, Marburg virus, Variola major virus (Smallpox virus), Variola minor (Alastrim), and Yersinia pestis*'' in their place.

(a) * * *

(3) Have the appropriate training and expertise to competently implement and manage the requirements of this part;

* * * * *

(6) Have their principal duty station at the physical location of the entity; and

* * * * *

(b) An entity may designate one or more individuals to serve as an alternate Responsible Official, who acts for the Responsible Official in his/her absence.

* * *

* * * * *

9. Section 73.10 is amended as follows:

a. By redesignating paragraphs (e) through (j) as paragraphs (f) through (k) respectively.

b. By adding a new paragraph (e) to read as set forth below.

c. In newly redesignated paragraph (g), by removing the words ''within any of the categories described in 18 U.S.C. 175b'' and adding the words ''a restricted person'' in their place.

d. In newly redesignated paragraph (j), by removing the word ''five'' and adding the word ''three'' in its place.

§ 73.10 Restricting access to select agents and toxins; security risk assessments.

* * * * *

(e) A person who has a valid approval from the HHS Secretary or Administrator for access to a select agent or toxin may request the HHS Secretary or Administrator to provide the person's approval status to another registered individual or entity for a specified period of time.

* * * * *

10. Section 73.11 is amended as follows:

a. By revising paragraph (b) to read as set forth below.

b. By revising paragraph (c)(2) to read as set forth below.

c. By adding new paragraphs (c)(8), (c)(9), and (c)(10) to read as set forth below.

d. By redesignating paragraphs (e) and (f) as paragraphs (f) and (g), respectively and by revising redesignated paragraph (f) to read as set forth below.

e. By adding a new paragraph (e) to read as set forth below.

§ 73.11 Security.

* * * * *

(b) The security plan must be designed according to a site-specific risk assessment and must provide graded protection in accordance with the risk of the select agent or toxin, given its intended use. A current security plan must be submitted for initial registration, renewal of registration, or when requested.

(c) * * *

(2) Contain provisions for the control of access to select agents and toxins, including the safeguarding of animals or plants intentionally or accidentally exposed to or infected with a select agent, against unauthorized access, theft, loss or release.

* * * * *

(8) Describe procedures for how the Responsible Official will be informed of suspicious activity that may be criminal in nature and related to the entity, its personnel, or its select agents or toxins; and how the Responsible Official will notify the Federal Bureau of Investigation (FBI) of such activity,

(9) Contain provisions for information security that:

(i) Ensure that all external connections to systems which control security of the facility are isolated or have controls that permit and monitor for only authorized and authenticated user access;

(ii) Ensure that authorized and authenticated users are only granted access to select agent and toxin related information, files, equipment (e.g., servers or mass storage devices) and applications as necessary to fulfill their roles and responsibilities, and that access is modified when the user's roles and responsibilities change or when their access to select agent and toxin is suspended or revoked;

(iii) Ensure that controls are in place that are designed to prevent malicious code (such as, but not limited to, computer virus, worms, spyware) from compromising the confidentiality, integrity, or availability of information systems;

(iv) Establish a robust configuration management practice for information systems to include regular patching and updates made to operating systems and individual applications; and

(v) Establish procedures that provide backup security measures in the event that access control systems and/or surveillance devices are rendered inoperable.

(10) Contain provisions and policies for shipping, receiving, and storage of select agents and toxins, including documented procedures for receiving, monitoring, and shipping of all select agents and toxins. These provisions must provide that an entity will properly secure containers on site and have a written contingency plan for unexpected shipments.

* * * * *

(e) In addition to the requirements contained in paragraphs (c) and (d) of this section, the security plan for an individual or entity possessing a Tier 1 select agent or toxin must also:

(1) Describe procedures for conducting a pre-access suitability assessment of persons who will have access to a Tier 1 select agent or toxin;

(2) Describe procedures for how an entity's Responsible Official will coordinate their efforts with the entity's safety and security professionals to ensure security of Tier 1 select agents and toxins and share, as appropriate, relevant information; and

(3) Describe procedures for the ongoing assessment of the suitability of personnel with access to a Tier 1 select agent or toxin. The procedures must include:

(i) Self- and peer-reporting of incidents or conditions that could affect an individual's ability to safely have access to or work with select agents and toxins, or to safeguard select agents and toxins from theft, loss, or release;

(ii) The training of all entity employees on entity policies and procedures for reporting, evaluation, and corrective actions concerning the assessment of personnel suitability to access Tier 1 agents and toxins; and

(iii) The ongoing suitability monitoring of individuals with access to Tier 1 select agents and toxins.

(4) Entities with Tier 1 select agents and toxins must prescribe and/or implement the following security enhancements:

(i) Procedures that will limit access to registered space only to those approved by the HHS Secretary or the Administrator and meet the criteria of the entity's program that will ensure individuals with access approval to select agents and toxins are trustworthy and behaving in a manner that upholds public health and safety, security, and the integrity of the scientific enterprise.

(ii) Procedures that limit access to laboratory and storage facilities outside of normal business hours to only those specifically approved by the Responsible Official or designee;

(iii) Procedures for allowing visitors, their property, and vehicles at the entry and exit points to the registered space, or at other designated points of entry to the building, facility, or compound based on the entity's site-specific risk assessment;

(iv) A minimum of three barriers where each subsequent barrier is different and adds to the delay in reaching secured areas where select agents and toxins are used or stored. Barriers must be monitored in such a way as to detect and assess intentional and unintentional circumventing of established access control measures under all conditions (day/night, severe weather, etc.);

(v) All registered space or areas that reasonably afford access to the registered space must be protected by an intrusion detection system (IDS) unless physically occupied;

(vi) Personnel monitoring the IDS must be capable of evaluating and interpreting the alarm and alerting the designated security response force or law enforcement;

(vii) Provide backup power and energy sources to power information security networks and integrated access

controls and related systems during emergencies;

(viii) Response time for security forces or local police must not exceed 15 minutes from the time of an intrusion alarm or report of a security incident;

(ix) Entities must conduct complete inventory audits of all Tier 1 select agents and toxins in long-term storage when any of the following occur:

(A) Upon the physical relocation of a collection or inventory of select agents or toxins for those Tier 1 select agents or toxins in the collection or inventory;

(B) Upon the departure or arrival of a principal investigator for those Tier 1 select agents and toxins under the control of that principal investigator; or

(C) In the event of a theft or loss of a Tier 1 select agent or toxin.

(5) Entities that possess Variola major virus and Variola minor virus must have the following additional security requirements:

(i) Require personnel with access to Variola major or Variola minor virus to have a Top Secret security clearance,

(ii) Require Variola major or Variola minor virus storage locations be under the surveillance of closed circuit television that is monitored,

(iii) After hours access procedures for Variola major or Variola minor virus must require notification of the entity's security staff prior to entry into the Variola laboratory and upon exit,

(iv) Require that observation zones be maintained in outdoor areas adjacent to the physical barrier at the perimeter of the entity and be large enough to permit observation of the activities of people at that barrier in the event of its penetration,

(v) Provide for a minimum of four barriers for the protection of the Variola major or Variola minor virus, one of which must be a perimeter fence,

(vi) Require a numbered picture badge identification subsystem to be used for all individuals who are authorized to access Variola major or Variola minor without escort,

(vii) Require the use, at all times, of properly trained, and equipped security force personnel able to interdict threats identified in the site specific risk assessment,

(viii) Identify security force personnel designated to strengthen onsite response capabilities, and that will be onsite and available at all times to carry out their assigned response duties,

(ix) Provide for security patrols to periodically check external areas of the registered areas to include physical barriers and building entrances,

(x) Require that all on-duty security force personnel shall be capable of maintaining continuous communication with support and response assets by way of security operations center,

(xi) Require that Variola major and Variola minor material in long term storage be stored in tamper-indicating containers,

(xii) Require that all spaces containing working or permanent Variola major or Variola minor stocks be locked and protected by an intrusion alarm system that will alarm upon the unauthorized entry of a person anywhere into the area,

(xiii) Require that alarms required pursuant to this section annunciate in a continuously manned security operations center located within the facility,

(xiv) Require that the security operations center shall be located within a building so that the interior is not visible from the perimeter of the protected area.

(f) In developing a security plan, an individual or entity should consider the documents entitled, ''Select Agents and Toxins Security Information Document'' and ''Select Agents and Toxins Security Plan Template.'' These documents are available on the Internet at *http://www.selectagents.gov/.*

* * * * *

11. Section 73.12 is amended as follows:

a. By revising paragraph (a) to read as set forth below.

b. By revising paragraph (c)(1) to read as set forth below.

c. In paragraph (c)(3), by removing the URL ''*http://www.cdc.gov/*'' and adding in its place ''*http://www.selectagents.gov*''.

d. By redesignating paragraph (d) as paragraph (e).

e. By adding a new paragraph (d) to read as set forth below.

§ 73.12 Biosafety.

* * * * *

(a) An individual or entity required to register under this part must develop and implement a written biosafety plan that is commensurate with the risk of the select agent or toxin, given its intended use. The biosafety plan must contain sufficient information and documentation to describe the biosafety and containment procedures for the select agent or toxin, including any animals or plants intentionally or accidentally exposed to or infected with a select agent.

* * * * *

(c) * * *

(1) The CDC/NIH publication, ''Biosafety in Microbiological and Biomedical Laboratories.'' This document is available on the Internet at *http://www.selectagents.gov.*

* * * * *

(d) 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. The occupational health program may also be made available to individuals without access to Tier 1 select agents and toxins.

* * * * *

§ 73.13 [Amended]

12. Section 73.13 is amended as follows:

a. In paragraph (a), in the introductory text, by adding the phrase '', or possess products (i.e. select agents that are not known to acquire the resistance naturally, if such acquisition could compromise the use of the drug to control disease agents in humans, veterinary medicine, or agriculture, or recombinant and or synthetic DNA containing genes for the biosynthesis of select toxins lethal for vertebrates at an LD[50] < 100 ng/kg body weight) resulting from,'' after the word ''conduct'' both times it appears.

b. In paragraph (b)(1), by removing the words ''Experiments utilizing recombinant DNA that involve the deliberate transfer of'' and replacing them with the words ''Experiments that involve the deliberate transfer of, or selection for,''.

c. In paragraph (b)(2), by adding the words ''synthetic or'' before the word ''recombinant.''

13. Section 73.14 is amended as follows:

a. By revising paragraph (a) to read as set forth below.

b. By revising paragraph (b) to read as set forth below.

c. By redesignating paragraph (c) and (d) as paragraphs (d) and (f) respectively.

d. By adding a new paragraph (c) to read as set forth below.

e. By adding a new paragraph (e) to read as set forth below.

§ 73.14 Incident response.

(a) An individual or entity required to register under this part must develop and implement a written incident response plan based upon a site specific risk assessment.[2] The incident response plan must be coordinated with any entity-wide plans, kept in the

[2] Nothing in this section is meant to supersede or preempt incident response requirements imposed by other statutes or regulations.

workplace, and available to employees for review.

(b) The incident response plan must fully describe the entity's response procedures for the theft, loss, or release of a select agent or toxin; inventory discrepancies; security breaches (including information systems); severe weather and other natural disasters; workplace violence; bomb threats and suspicious packages; and emergencies such as fire, gas leak, explosion, power outage, etc.

(c) The response procedures must account for hazards associated with the select agent or toxin and appropriate actions to contain such select agent or toxin, including any animals or plants intentionally or accidentally exposed to or infected with a select agent.

* * * * *

(e) Entities with Tier 1 select agents and toxins must have the following additional incident response policies or procedures:

(1) The incident response plan must fully describe the entity's response procedures for failure of intrusion detection or alarm system; and

(2) The incident response plan must describe notification procedures for the FBI in the event of a theft or suspicious activity that may be criminal in nature involving a Tier 1 select agent or toxin.

* * * * *

14. Section 73.15 is revised to read as follows:

§ 73.15 Training.

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

(1) To each individual with access approval from the HHS Secretary or Administrator before that individual has such access to select agents and toxins. The training must address the particular needs of the individual, the work they will do, and the risks posed by the select agents or toxins.

(2) To each individual not approved for access to select agents and toxins by the HHS Secretary or Administrator before that individual enters areas where select agents or toxins are handled or stored (e.g., laboratories, growth chambers, animal rooms, greenhouses, storage areas, shipping/receiving areas, production facilities, etc.). Training for escorted personnel must be based on the risk associated with accessing areas where select agents and toxins are used and/or stored.

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

(c) Refresher training must be provided annually or at such time as the registered individual or entity significantly amends its security, incident response, or biosafety plans.

(d) The Responsible Official must ensure a record of the training provided to each individual with access to select agents and each escorted individual (e.g., laboratory workers, visitors, etc.) is maintained. The record must include the name of the individual, the date of the training, a description of the training provided, and the means used to verify that the employee understood the training.

15. Section 73.16 is amended as follows:

a. By redesignating paragraph (f), (g), (h), and (i) as paragraphs (i), (j), (k), and (g) respectively.

b. In redesignated paragraph (g), by removing the words ''packaging and''.

c. By adding a new paragraph (f) to read as set forth below.

d. By adding a new paragraph (h) to read as set forth below.

e. By adding a new paragraph (l) to read as set forth below.

§ 73.16 Transfers.

* * * * *

(f) After authorization is provided by APHIS or CDC, the select agent(s) and toxin(s) are packaged for shipment in compliance with all applicable laws concerning packaging by 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.

* * * * *

(h) 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.

* * * * *

(l) A registered individual or entity transferring an amount of a HHS toxin otherwise excluded under the provisions of § 73.3(d) of this part must:

(1) Transfer the HHS toxin only after using due diligence and documenting that the recipient has a legitimate need (reasonably justified by a prophylactic, protective, bona fide research, or other peaceful purpose) to handle or use such toxins. The HHS Secretary retains the authority to, without prior notification, inspect and copy or request the submission of the due diligence documentation to the CDC.

(2) Report to CDC any known or suspected violation of Federal law or suspicious activity related to the toxin.

16. Section 73.17 is amended as follows:

a. By revising paragraph (a)(1) introductory text to read as set forth below.

b. By redesignating paragraphs (a)(2) through (a)(6) as paragraphs (a)(3) through (a)(7) respectively.

c. By adding a new paragraph (a)(2) to read as set forth below.

§ 73.17 Records.

(a) * * *

(1) An accurate, current inventory for each select agent (including viral genetic elements, recombinant and/or synthetic nucleic acids, and recombinant and/or synthetic organisms) held in long-term storage (placement in a system designed to ensure viability for future use, such as in a freezer or lyophilized materials), including:

* * * * *

(2) An accurate, current inventory of any animals or plants intentionally or accidentally exposed to or infected with a select agent (including number and species, location, and appropriate disposition);

* * * * *

17. Section 73.20 is revised to read as set forth below.

§ 73.20 Administrative review.

(a) An individual or entity may appeal a denial, revocation, or suspension of registration under this part. The appeal must be in writing, state the factual basis for the appeal, and be submitted to the HHS Secretary within 30 calendar days of the decision.

(b) An individual may appeal a denial, limitation, or revocation of access approval under this part. The appeal must be in writing, state the factual basis for the appeal, and be submitted to the HHS Secretary within 180 calendar days of the decision.

(c) The HHS Secretary's decision constitutes final agency action.

Dated: September 21, 2011.

Kathleen Sebelius,

Secretary.

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