**DEPARTMENT OF AGRICULTURE**

**Animal and Plant Health Inspection Service**

**7 CFR Part 331**

**9 CFR Part 121**

**[Docket No. APHIS–2009–0070]**

**RIN 0579–AD09**

# Agricultural Bioterrorism Protection Act of 2002; Biennial Review and Republication of the Select Agent and Toxin List; Amendments to the Select Agent and Toxin Regulations

**AGENCY:** Animal and Plant Health Inspection Service, USDA.

**ACTION:** Final rule.

**SUMMARY:** In accordance with the Agricultural Bioterrorism Protection Act of 2002, we are amending and republishing the list of select agents and toxins that have the potential to pose a severe threat to animal or plant health, or to animal or plant products. The Act requires the biennial review and republication of the list of select agents and toxins and the revision of the list as necessary. This action implements the findings of the third biennial review of the list. In addition, we are reorganizing the list of select agents and toxins based on the relative potential of each select agent or toxin to be misused to adversely affect human, plant, or animal health. Such tiering of the list allows for the optimization of security measures for those select agents or toxins that 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. We are also making a number of amendments to the regulations, including the addition of definitions and clarification of language concerning security, training, biosafety, biocontainment, and incident response. These changes will increase the usability of the select agent regulations as well as provide for enhanced program oversight.

**DATES:** The amendments to 7 CFR 331.1 through 331.10, 331.13, and 331.16 through 331.20 and 9 CFR 121.1 through 121.10, 121.13, 121.16, 121.17, and 121.20 are effective December 4, 2012. The remaining provisions of this final rule are effective April 3, 2013.

**FOR FURTHER INFORMATION CONTACT:** Mr. Charles L. Divan, Acting Director, APHIS Agriculture Select Agent Program, APHIS, 4700 River Road Unit 2, Riverdale, MD 20737–1231; (301) 851–3300, option 1.

**SUPPLEMENTARY INFORMATION:**

## Executive Summary

On July 29, 2010, we published in the **Federal Register** (75 FR 44724–44725, Docket No. APHIS–2009–0070) an advance notice of proposed rulemaking and request for comments (ANPR)[1] and On October 3, 2011, we published in the **Federal Register** (76 FR 61228–61244, Docket No. APHIS–2009–0070) a proposal[2] regarding our intent to amend and republish the list of select agents and toxins that have the potential to pose a severe threat to animal or plant health, or to animal or plant products, reorganize the list of select agents and toxins based on the relative potential of each select agent or toxin to be misused to adversely affect human, plant, or animal health, and amend the regulations in order to add definitions and clarify language concerning security, training, biosafety, biocontainment, and incident response.

Specifically, the ANPR solicited comments regarding whether there are other select agents or toxins that should be added to the Plant Protection and Quarantine (PPQ) and Veterinary Services (VS) lists of select agents and toxins, whether any of the select agents or toxins on the PPQ or VS lists should be removed, whether the PPQ and VS lists of select agents and toxins should be tiered based on the relative bioterrorism risk presented by each select agent or toxin, and whether the security requirements for select agents or toxins in the highest tier should be stratified based on type of use or other factors. Comments received as a result of the ANPR were used in order to inform our discussions on the content of the select agent list and our determination regarding reorganization of the list in the proposed rule. We solicited comments concerning our proposal for 60 days ending December 2, 2011. We reopened and extended the deadline for comments until January 17, 2012, in a document published in the **Federal Register** on December 15, 2011 (76 FR 77914, Docket No. APHIS–2009–0070). We received 30 comments by that date. They were from researchers, scientific organizations, laboratories, and universities.

Changes to the current regulations detailed in this final rule include:

1. Modification of the select agent and toxin list:

- The following agents would no longer be considered PPQ select agents or toxins, or would be excluded from compliance with the select agent regulations: Any subspecies of *Ralstonia solanacearum* except race 3, biovar 2 and all subspecies of *Sclerophthora rayssiae* except var. *zeae, and Xylella fastidiosa,* citrus variegated chlorosis (CVC) strain.
- The following agents would no longer be considered VS select agents or toxins, or would be excluded from compliance with the select agent regulations: Any low pathogenic strains of avian influenza virus, any strain of Newcastle disease virus which does not meet the criteria for virulent Newcastle disease virus, all subspecies *Mycoplasma capricolum* except subspecies *capripneumoniae* (contagious caprine pleuropneumonia), and all subspecies *Mycoplasma mycoides* except subspecies *mycoides* small colony (*Mmm* SC) (contagious bovine pleuropneumonia), Akabane virus; Bluetongue virus (exotic), Bovine spongiform encephalopathy agent; Camel pox virus; *Ehrlichia ruminantium* (Heartwater); Japanese encephalitis virus; Malignant catarrhal fever virus (Alcelaphine herpesvirus type 1); Menangle virus; and Vesicular stomatitis virus (exotic): Indiana subtypes VSV–IN2, VSV–IN3.
- The following agent would no longer be considered a VS/Department of Health and Human Services (HHS) overlap select agent: Venezuelan Equine Encephalitis Virus (subtypes ID and IE).

2. Tiering of the select agent and toxin lists:

Tier 1 select agents and toxins:

- PPQ select agents and toxins: None.
- VS select agents and toxins: Foot-and-mouth disease virus and Rinderpest virus.
- VS/HHS overlap select agents and toxins: *Bacillus anthracis, Burkholderia mallei,* and *Burkholderia pseudomallei.*

3. Establishing physical security standards for entities possessing Tier 1 select agents and toxins, including the requirement to conduct pre-access assessments and ongoing monitoring of personnel with access to Tier 1 agents and toxins;

4. Miscellaneous revisions to the regulations to clarify regulatory language concerning security, training, biosafety, and incident response.

*Costs of the Rule:* Entities affected by the rule include research and diagnostic facilities; Federal, State, and university laboratories; and private commercial and non-profit enterprises. The regulations require registering the

[1] To view the ANPR and the comments we received, go to *http://www.regulations.gov/#!docketDetail;D=APHIS–2009–0070.*

[2] To view the proposed rule and the comments we received, go to *http://www.regulations.gov/#!docketDetail;D=APHIS–2009–0070.*

possession, use, and transfer of select agents or toxins. In addition, the entity is required to ensure that the facility where the agent or toxin is housed has adequate biosafety and containment measures, that the physical security of the premises is adequate, that all individuals with access to select agents or toxins have the appropriate education, training, and/or experience to handle such agents or toxins, and that complete records concerning activities related to the select agents or toxins are maintained.

The rule will further reduce or minimize the risk of misuse of select agents and toxins that have the potential to pose a severe threat to human, animal or plant health, or to animal or plant products. APHIS and HHS recognize that several of the required measures of the regulations may impose certain operational costs upon affected entities, particularly entities that have the newly designated Tier 1 select agents and toxins. In many cases, however, the affected entities already employ some or all of the required measures. Compliance costs actually incurred will therefore vary from one entity to the next.

While information on the specific changes that would need to occur at individual sites and the associated costs was not readily available during proposed rulemaking, some general observations regarding the potential costs were presented. These general cost observations can be found in Table 2 of the Regulatory Impact Analysis located at: *www.regulations.gov* and at *http://www.selectagents.gov*.

*Benefits of the Rule:* The objectives of the final rule is to create a means of ensuring enhanced oversight in the transfer, storage, and use of select agents and toxins; define the security procedures and suitability assessments for pre-access suitability and continual monitoring of individuals with access to Tier 1 select agents and toxins; and require that entities in possession of such agents and toxins develop and implement effective means of biosafety, information security, and physical security. The overall benefit of the amended provisions will be a reduced likelihood of the accidental or intentional release of a select agent or toxin and the avoidance of costs associated with such a release. The goal of the amended regulations is to enhance the protection of human, animal, and plant health and safety.

**Background**

The Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (referred to below as the Bioterrorism Response Act) provides for the regulation of certain biological agents that have the potential to pose a severe threat to both human and animal health, to animal health, to plant health, or to animal and plant products. The Animal and Plant Health Inspection Service (APHIS) has the primary responsibility for implementing the provisions of the Act within the Department of Agriculture (USDA). 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. Plant Protection and Quarantine (PPQ) select agents and toxins are those that have the potential to pose a severe threat to plant health or plant products. Overlap select agents and toxins are those that have been determined to pose a severe threat to human and animal health or animal products. Overlap select agents are subject to regulation by both APHIS and the Centers for Disease Control and Prevention (CDC), which has the primary responsibility for implementing the provisions of the Act for the Department of Health and Human Services (HHS).

Subtitle B (which is cited as the ''Agricultural Bioterrorism Protection Act of 2002'' and referred to below as the Act), section 212(a), provides, in part, that the Secretary of Agriculture (the Secretary) must establish by regulation a list of each biological agent and each toxin that the Secretary determines has the potential to pose a severe threat to animal or plant health, or to animal or plant products. Paragraph (a)(2) of section 212 requires the Secretary to review and republish the list every 2 years and to revise the list as necessary. In this document, we are amending and republishing the list of select agents and toxins based on the findings of our third biennial review of the list.

In determining whether to include an agent or toxin on the list, the Act requires that the following criteria be considered:

- The effect of exposure to the agent or the toxin on animal and plant health, and on the production and marketability of animal or plant products;
- The pathogenicity of the agent or the toxin and the methods by which the agent or toxin is transferred to animals or plants;
- The availability and effectiveness of pharmacotherapies and prophylaxis to treat and prevent any illness or disease caused by the agent or toxin; and
- Any other criteria that the Secretary considers appropriate to protect animal or plant health, or animal or plant products.

We use the term ''select agents and toxins'' throughout the preamble of this final rule. Unless otherwise specified, the term ''select agents and toxins'' will refer to all agents or toxins listed by APHIS. When it is necessary to specify the type of select agent or toxin, we will use the following terms: ''PPQ select agents and toxins'' (for the plant agents and toxins listed in 7 CFR 331.3), ''VS select agents and toxins'' (for the animal agents and toxins listed in 9 CFR 121.3), or ''overlap select agents and toxins'' (for the agents and toxins listed in both 9 CFR 121.4 and 42 CFR 73.4).

On October 3, 2011, we published in the **Federal Register** (76 FR 61228–61244, Docket No. APHIS–2009–0070) a proposal [3] to amend and republish the list of select agents and toxins that have the potential to pose a severe threat to animal or plant health, or to animal or plant products, reorganize the list of select agents and toxins based on the relative potential of each select agent or toxin to be misused to adversely affect human, plant, or animal health, and amend the regulations in order to add definitions and clarify language concerning security, training, biosafety, biocontainment, and incident response.

We solicited comments concerning our proposal for 60 days ending December 2, 2011. We reopened and extended the deadline for comments until January 17, 2012, in a document published in the **Federal Register** on December 15, 2011 (76 FR 77914, Docket No. APHIS–2009–0070). We received 30 comments by that date. They were from researchers, scientific organizations, laboratories, and universities. They are discussed below by topic.

**Guidance Documents**

In the proposed rule, we specifically requested comment from the regulated community and any other interested persons on the need for and desirability of guidance documents that would serve to assist regulated entities in meeting the requirements of regulations. We were particularly interested in public comment regarding Web sites, articles, or other sources useful in developing such guidance documents. We received a number of comments on the issue of guidance, which are discussed below.

Two commenters suggested the use of specific documents in creating guidance: The Laboratory Biorisk Management Standard, which was

[3] To view the proposed rule and the comments we received, go to *http://www.regulations.gov/#!docketDetail;D=APHIS-2009-0070.*

developed by the European Committee for Standardization, and the report ''Guidance for Enhancing Personnel Reliability and Strengthening the Culture of Responsibility,'' which was developed by the National Science Advisory Board for Biosecurity.

We agree with the commenters and have utilized both sources in developing guidance.

One commenter stated that the select agent program should develop a standardized template that addresses each item required by the regulations, both for regulated entities and inspectors. The commenter went on to say that the templates should be posted on the select agent Web site.

The National Select Agent Registry at www.selectagents.gov includes checklists, guidance documents, and templates that we have developed to aid entities in meeting the requirements of the regulations. The select agent program also conducts regular inspector training in order to standardize inspector understanding of the regulations and inspection process. We accept entity feedback regarding the inspection process and incorporate it into our training program as appropriate.

Another commenter stated that the involvement of regulated entities in the development of guidance is crucial, as it will ensure that the new regulations may be implemented without unsustainable increases in cost to those entities.

The guidance documents developed in conjunction with this rule are, in part, a response to the questions and issues raised by the commenters regarding various aspects of the proposed rule. We also consulted HHS and USDA subject matter experts and other sources including National Science Advisory Board for Biosecurity, the National Academies, the Department of Defense Security Engineering Facilities Planning Manual, and Director of Central Intelligence Directive Number 6/9. Regarding the commenter's cost concerns, the guidance developed by the select agent program does not set out a prescriptive series of procedures that must be followed by all regulated entities; rather, it establishes examples of ways in which an entity may choose to meet the requirements of the regulations. We have purposefully left the regulations in their general state in order to allow for the wide variety of regulated entities to meet the regulatory standard in a way that is most cost-effective for each.

**PPQ Select Agents and Toxins**

We proposed to amend the list of PPQ select agents and toxins listed in 7 CFR 331.3 by removing *Xylella fastidiosa,* citrus variegated chlorosis (CVC) strain, from the list as it no longer meets the criteria for use as an agroterrorism agent.

One commenter stated that the scientific basis for the removal of *Xylella fastidiosa* from the list was unclear and requested clarification concerning our decision. The commenter additionally stated that if the review process for such removal were to be transparent, with expert opinion from the public and private sector, including a sound scientific analysis and an assessment of the biosecurity risk of each agent, other plant pathogens on the list of select agents and toxins could potentially be removed.

We are making no changes as a result of this comment. Each agent on the select agent and toxin list was considered for retention or removal based on a variety of factors, including, but not limited to, the scientific concerns cited by the commenter. Further, the select agent program did employ subject-matter experts as part of the decision-making process as recommended by the commenter in addition to soliciting public comment. Experts in the biology of these agents and toxins evaluated their ''potential for mass casualties or devastating effects to the economy, critical infrastructure, or public confidence.'' This evaluation included assessments of morbidity and mortality, communicability, low infectious dose, availability of countermeasures, and economic impact of a potential attack. Each agent and toxin was then assessed for its ''risk of deliberate misuse,'' including its history of weaponization and/or known interest by State or non-State adversaries. These evaluations, combined with input received as a result of the publication of an advance notice of proposed rulemaking and request for comments (ANPR) [4] in the **Federal Register** on July 29, 2010, and relevant findings in recent government and non-government reports, formed the basis for deliberations concerning which agents should constitute the list. It is important to note that removal of pathogens from the list of select agents and toxins does not mean that they are not of potential concern, but rather that the risk they represent has been reevaluated using the above criteria. Reduction of the list is meant to decrease the burden on researchers and focus attention on agents and toxins judged to be of greatest biosecurity concern.

The list of PPQ select agents and toxins includes an entry for *Xanthomonas oryzae.* While we did not propose any changes to the entry for *Xanthomonas oryzae,* one commenter stated that it should be removed from the list of select agents and toxins and offered a number of arguments, which are discussed below.

The commenter proposed the removal of *Xanthomonas oryzae* based on the assertion that *Xanthomonas oryzae* populations are adapted only to local conditions and do not persist upon introduction to new environments. Given that the major natural host for *Xanthomonas oryzae* is rice, the commenter also compared cultivation practices utilized in domestic commercial rice production with those utilized in Asian commercial rice production. The commenter argued that domestic commercial cultivation practices eliminate transmission of the pathogen since rice seeds are directly planted whereas in Asia rice seedlings are cultivated elsewhere and then transplanted, and wounds created during such handling and transplant are important modes of transmission for the pathogen to healthy seedlings. In addition, the commenter said that domestic weather patterns are not conducive to dissemination and that quarantines can prevent seed-borne disease. The commenter claimed that field-to-field spread of *Xanthomonas oryzae* in Asia is largely dependent on the strong winds and driving rains that occur frequently during typhoon season.

We are making no changes to the regulations as a result of this comment. Natural spread or persistence of the pathogen in a particular location is not at issue; it is the risk of deliberate misuse leading to the most significant potential for mass casualties or devastating effects to the economy, critical infrastructure, or public confidence. The issue of standard commercial planting practices for rice in a domestic versus Asian setting is not relevant to the discussion of *Xanthomonas oryzae*'s potential for use as a biological weapon. APHIS analyzed and assessed this pathogen using the criteria discussed earlier in this document. Based on that analysis and assessment and the knowledge that *Xanthomonas oryzae* has been modified for use as a biological weapon in the past, it has been retained on the list of PPQ select agents and toxins.

The commenter also stated that *Xanthomonas oryzae* should be

[4] To view the ANPR and the comments we received, go to *http://www.regulations.gov/#!docketDetail;D=APHIS-2009-0070.*

removed from the list of select agents and toxins because it is endemic in the United States and any foreign strains introduced in the future would prove unlikely to establish and spread.

While we disagree with the commenter's assertion regarding *Xanthomonas oryzae's* pathogenicity, these arguments are unrelated to the work of the select agent program as a whole as the select agent regulations do not allow for the environmental release of listed agents and toxins. Whether or not a given select agent or toxin is endemic in the United States is not the only determining factor in the select agent or toxin's inclusion on the list. The regulations govern use of listed select agents and toxins in laboratory settings only. In this regard, the case for maintaining *Xanthomonas oryzae* on the list of those select agents and toxins whose deliberate misuse represents the most significant potential for mass casualties or devastating effects to the economy, critical infrastructure, or public confidence, is compelling as work was done on *Xanthomonas oryzae* in the 1970s which led to its classification as a bioterrorism agent by the security community.

The list of PPQ select agents and toxins includes an entry for *Ralstonia solanacearum,* race 3, biovar 2. While we did not propose any changes to the entry for *Ralstonia solanacearum,* race 3, biovar 2, five commenters stated that it should be removed from the list of select agents and toxins.

The commenters argued that, based on the biological and historical climate data for North America, *Ralstonia solanacearum,* race 3, biovar 2 does not have the potential to pose a severe threat to plant health or plant products in the context of U.S. agriculture. The commenters stated that *Ralstonia solanacearum,* race 3, biovar 2 is only a serious problem in the developing world in those areas of cool highland tropics where annual temperature profiles differ significantly from those found in the major potato growing regions in the United States (i.e., Colorado, Idaho, Maine, Minnesota, North Dakota, and Wisconsin). The commenters argued that, unlike the northern States, the cool highland tropics experience few hard freezes and no long winters. Since, the commenters claimed, epidemiological and laboratory research data show that *Ralstonia solanacearum,* race 3, biovar 2 is intolerant of freezing and freeze-thaw cycles and does not generally survive winters in regions with sustained low temperatures, the bacterium is unlikely to become established in the northern U.S. where potatoes are commercially grown.

We disagree with the commenters' claim that *Ralstonia solanacearum,* race 3, biovar 2 is only a serious pathogen in the developing world as the bacterium has been shown to establish itself in northern Europe by over-wintering in weeds, thereby posing a severe threat to *Solanaceae* species (e.g., potato, eggplant, and tomato) in cool climates such as those found both in northern Europe and North America. In addition, as discussed earlier in this document, the evaluation process for select agents includes broad criteria that not only focus on the biological characteristics of a given pathogen, but also that pathogen's ability to produce a devastating effect on the economy and the threat that pathogen represents if it were to be used as a biological weapon. We are making no changes as a result of these comments.

The commenters also stated that retaining *Ralstonia solanacearum,* race 3, biovar 2 on the list of select agents and toxins would further constrain research in the field of *Ralstonia* research. The commenters attributed such listing with registration time for use, transfer, or possession of select agents and toxins in excess of 18 months prior to the initiation of research and difficulty in meeting the registration requirements.

We are making no changes in response to these comments. While there are added requirements concerning physical security, personnel authorization, recordkeeping, biocontainment, and site inspections, we do not believe these requirements will impede research as, in many cases these regulations serve to codify systems and procedures already in use by a majority of regulated entities. Further, entity registration for use, transfer, or possession of select agents and toxins does not take, nor has ever taken, 18 months. On average, new entity registration takes 6 months from the date the request is received by the select agent program and the issuance of the registration certificate. The security risk assessment (SRA) takes less than 45 days and runs parallel to the entity registration process. These timeframes are all based on the assumption that the entity registration submission and the SRA submission are complete and accurate for select agent program review prior to the required on-site inspection.

Commenters additionally stated that *Ralstonia solanacearum,* race 3, biovar 2 should be removed from the list for the same reasons that were cited for the proposed removal of *Xylella fastidiosa,* CVC strain.

We are making no changes as a result of these comments. The decision to remove the CVC strain from the list of select agents and toxins was based on the completion of extensive review and analysis of the criteria for inclusion on the list. In particular, the creation of detection methods and the use of geostatistical analysis with relation to monitoring in order to facilitate a response to any purposeful introduction are both key components in our decision to delist CVC. As discussed earlier in this document, the evaluation process for select agents includes a broad number of criteria that not only focus on the biological characteristics of a given pathogen but also that pathogen's ability to produce a devastating effect on the economy and the threat that pathogen represents if it were to be used as a biological weapon. Based on that analysis and assessment *Ralstonia solanacearum,* race 3, biovar 2 will remain on the list of select agents and toxins.

Commenters said that eradicating *Ralstonia solanacearum,* race 3, biovar 2 introduced into the United States through infected geraniums cost commercial greenhouses and importers millions of dollars as a direct result of its presence on the list of select agents and toxins.

We are making no changes as a result of these comments. The presence of *Ralstonia solanacearum,* race 3, biovar 2 on the list of select agents and toxins had no bearing on the eradication program instituted by APHIS. The cost of this eradication program to commercial greenhouses and importers was the same as the cost of eradicating any other quarantine plant pathogen not known to be present in the United States.

**Identification of Strains**

The list of VS select agents and toxins includes an entry for virulent Newcastle disease virus. While we did not propose any changes to the entry for virulent Newcastle disease virus, one commenter stated that, by not considering all forms of Newcastle disease virus as select agents, APHIS has created a period of uncertainty prior to the completion of the sequencing necessary to identify whether a form of Newcastle disease virus is virulent or not. The commenter requested clarification as to whether laboratories would be required to treat uncharacterized Newcastle disease virus as a select agent given this uncertainty.

We agree with the commenter's point. We have therefore revised the list of VS only select agents and toxins in order to list certain select agents and toxins not by specific strains but by the generic

taxonomic classifications for those select agents. The specific VS only select agents and toxins affected are: Avian influenza virus (highly pathogenic), *mycoplasma capricolum* subspecies *capripneumoniae* (contagious caprine pleuropneumonia), *mycoplasma mycoides* subspecies *mycoides* small colony (*Mmm* SC) (contagious bovine pleuropneumonia), and virulent Newcastle disease virus, which we have altered to read avian influenza virus, *mycoplasma capricolum, mycoplasma mycoides,* and Newcastle disease virus, respectively. In order to capture the applicable strains, subtypes, or pathogenicity levels we have also added exemptions for those strains, subtypes, or pathogenicity levels of certain select agents and toxins which are not considered to have the potential to pose a severe threat to animal health or animal products.

The list of overlap select agents and toxins contains an entry for Venezuelan equine encephalitis. One commenter stated that, by not considering all subtypes of Venezuelan equine encephalitis as select agents, APHIS has created a period of uncertainty prior to the completion of the typing necessary to identify whether a form of Venezuelan equine encephalitis is among the subtypes classified by APHIS as select agents. The commenter requested clarification as to whether laboratories would be required to treat untyped Venezuelan equine encephalitis as a select agent given this uncertainty.

We agree with the commenter's point. As stated previously, we have therefore revised the list of overlap select agents and toxins in order to list certain select agents and toxins not by specific strains but by the generic taxonomic classifications for those select agents. The specific overlap select agent is Venezuelan equine encephalitis virus: Epizootic Subtypes IAB, IC, which we have altered to read Venezuelan equine encephalitis virus. In order to capture the applicable strains, subtypes, or pathogenicity levels we have also added exemptions for those strains, subtypes, or pathogenicity levels of certain select agents and toxins which are not considered to have the potential to pose a severe threat to animal or human health or animal products. We do note that we have specifically included *Bacillus anthracis* (Pasteur strain) in the list of overlap select agents and toxins. This is necessary in order to distinguish this strain, which we do not consider to be a Tier 1 select agent, from all other strains of *Bacillus anthracis,* which are classified as Tier 1 select agents.

Although we did not receive any comments on this issue as it concerns PPQ only select agents and toxins, in order to strengthen the regulations as discussed previously as well as to maintain parity between the VS and PPQ regulations, we are revising the list of PPQ only select agents and toxins in order to list certain select agents and toxins not by specific strains but by the generic taxonomic classifications for those select agents. The specific PPQ only select agents and toxins affected are: *Ralstonia solanacearum,* race 3, biovar 2 and *Sclerophthora rayssiae* var. *zeae* which we have altered to read *Ralstonia solanacearum* and *Sclerophthora rayssiae,* respectively. In order to capture the applicable strains, subtypes, or pathogenicity levels we have also added exemptions for those strains, subtypes, or pathogenicity levels of certain select agents and toxins which are not considered to have the potential to pose a severe threat to plant health or plant products.

With the changes described above, we clearly establish that when an agent or toxin is initially identified to a taxonomic level, in the case of an agent, or by its toxicological properties, in the case of a toxin, it is regulated under the select agent regulations until further testing is accomplished to exclude the particular agent by strain, subtype, pathogenicity levels, or a particular toxin by properties. We believe it is important that laboratories treat these agents as select agents until further testing can be conducted to verify whether the agent is of a strain, subtype, or pathogenicity level that presents a higher level of danger to animal health and safety. These changes will not have any impact on the exemption for diagnostic laboratories or alter the process of receiving diagnostic samples and forwarding any potentially identified select agents for further testing. They also do not change the reporting criteria for those agents confirmed to be select agents. Finally, they do not change the current lists of select agents and toxins but alters the fashion in which select agents and toxins are listed with specific exemptions included to ensure that appropriate verification of the agents by strains, subtypes, or pathogenicity level occurs.

**VS Select Agents and Toxins**

We proposed to remove nine VS select agents and toxins from the list set out in § 121.3(b). Specifically, we proposed to remove the following: Akabane virus; Bluetongue virus (exotic), Bovine spongiform encephalopathy agent; Camel pox virus; *Ehrlichia ruminantium* (Heartwater); Japanese encephalitis virus; Malignant catarrhal fever virus (Alcelaphine herpesvirus type 1); Menangle virus; and Vesicular stomatitis virus (exotic): Indiana subtypes VSV–IN2, VSV–IN3.

One commenter recommended that we exclude the Texas GB strain of Newcastle disease virus from select agent status. The commenter stated that the exclusion is warranted since, although Newcastle disease virus is widespread in the environment, there is little illness if a flock is exposed because nearly all commercial poultry is vaccinated against the disease. The commenter observed that the Texas GB strain of Newcastle disease virus is used by vaccine manufacturers as the challenge organism to verify the potency of Newcastle disease virus vaccines and this fact gives poultry producers a high degree of assurance that their flocks are protected against the Texas GB strain. Given these factors, the commenter concluded that the Texas GB strain is not a biosecurity threat to the domestic poultry industry, and the strain should be excluded from APHIS's definition of virulent Newcastle disease virus.

We are making no change in this final rule as a result of this comment. Texas GB strain of Newcastle disease virus is a highly virulent form of Newcastle disease virus and, as such, is appropriately included in the general category of ''virulent Newcastle disease virus.'' While vaccine manufacturers do use the Texas GB strain of Newcastle disease virus as a challenge organism for Newcastle disease virus vaccines, this is on account of its high level of virulence. A vaccine effective against the Texas GB strain of Newcastle disease virus can therefore be assumed to be effective against less virulent forms of Newcastle disease virus.

The list of VS select agents and toxins includes an entry for avian influenza virus (highly pathogenic) (HPAI). While we did not propose any changes to the entry for HPAI, one commenter proposed that we change the guidance by which influenza strains are categorized as HPAI. The commenter argued that extensive evidence has been obtained to support the conclusion that, while the HA polybasic cleavage site is the primary determinant for HPAI strains, strains with removed HA polybasic cleavage sites have been created, tested, and ultimately excluded from select agent status. The commenter stated that, as a result of these experiments and history, APHIS should specify that avian influenza strains without the HA polybasic cleavage site are not HPAI viruses and, therefore, not subject to the select agent regulations.

The commenter further argued that continuing to consider strains of avian influenza with removed HA polybasic cleavage sites as select agents until such time as an exclusion is granted would impede vaccine availability in the event of an HPAI pandemic in either the human or avian population. The commenter stated that the lead candidates for the seed viruses that would be used to make vaccines against HPAI viruses during such an event will likely be attenuated strains with mutated polybasic cleavage sites. The commenter stated that the current process by which avian influenza strains that lack the polybasic cleavage site are granted exclusions takes weeks or months, an untenable timeline in the event of an HPAI pandemic.

We are making no changes in response to this comment. APHIS standards are based on existing internationally recognized requirements established by the World Animal Health Organization (OIE). In the event of a future HPAI pandemic such as the one described by the commenter, APHIS would work in conjunction with HHS to address any vaccine availability issues. Finally, attenuated strains of select agents officially approved for human vaccination purposes by the Food and Drug Administration (FDA) or other recognized national or international organizations continue to be exempt from the select agent regulations as specified by the regulations in § 121.5(c) and (d).

**Overlap Select Agents and Toxins**

We proposed to modify the list of overlap select agents and toxins by removing certain subtypes of Venezuelan equine encephalitis virus from the list of overlap select agents and toxins set out in 9 CFR 121.4(b), and to clarify that only Venezuelan equine encephalitis subtypes IAB and IC would remain on the list. These subtypes contain the only recognized strains of Venezuelan equine encephalitis that can suddenly affect a large number of animals over a large area (i.e., epizootic). The remaining subtypes, ID and IE, are strains prevalent among existing animal populations (i.e., enzootic) 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 list of overlap select agents and toxins.

Another commenter recommended that we remove Venezuelan equine encephalitis strain 3014 from the list of select agents and toxins. The commenter argued that, although strain 3014 was derived from a 1AB isolate, this molecularly cloned strain has properties that render it incapable of causing epizootic or epidemic transmission. The commenter stated that mutations selected after only a handful of passages make the virus avirulent in adult mice and dramatically increases its clearance from the bloodstream of mice following intravenous inoculation. Further, the vanishingly low titers of strain 3014 consist of envelope glycoprotein gene mutations, which allow the strain to bind heparin sulfate; such binding is also associated with the attenuated phenotype of Venezuelan equine encephalitis strain TC–83, which is also derived from the 1AB Trinidad donkey strain by passage in culture that has already been excluded from select agent status.

We are making no changes as a result of this comment. Since Venezuelan equine encephalitis strain 3014 is derived from a listed overlap select agent, the commenter's proposal for its removal is more appropriately addressed via the exclusion process for overlap select agents and toxins as detailed in 9 CFR 121.6. We have contacted the commenter and provided guidance regarding how they may initiate this process.

We proposed to designate *Bacillus anthracis* as a Tier 1 select agent. A number of commenters objected to such a blanket designation, arguing instead that the *Bacillus anthracis* Pasteur strain should be exempted from consideration both as a Tier 1 select agent and as a select agent in general.

One commenter argued that given the fact that Laboratory Response Network (LRN) laboratories maintain live cultures of non-pathogenic *Bacillus anthracis* Pasteur strain for use in quality control testing, designation of *Bacillus anthracis* as a Tier 1 select agent therefore has the potential to impact the willingness or ability of LRN laboratories to maintain inventories of *Bacillus anthracis* Pasteur strain due to the regulatory and financial burdens associated with possession of Tier 1 select agents and toxins. The commenter went on to state that this situation could potentially impact national health and safety given that the potential use of *Bacillus anthracis* spores as a bioweapon remains a viable threat and increased burdens, particularly on small laboratories, could lead to the overall decrease in the number of laboratories that would otherwise serve to ensure that the LRN has sufficient capacity to detect and respond to a deliberate release of *Bacillus anthracis.*

Three commenters stated that the *Bacillus anthracis* Pasteur strain is analogous to the *Bacillus anthracis* Sterne strain, which is excluded since it was determined not to pose a severe threat to public health and safety, animal health, or animal products. The commenter argued that *Bacillus anthracis* Pasteur strain should not be considered as a select agent given that the only way to create an agent that poses a severe threat would be via combination of the Pasteur strain with a non-regulated strain. The commenter pointed out that other agents that pose little harm individually, but could be modified genetically to become harmful are not included on the select agent list because of this potential threat.

Another commenter claimed that the designation of *Bacillus anthracis* Pasteur strain as a select agent would not serve to prevent an authorized person from intentionally or accidentally facilitating the combination of plasmids from Sterne and Pasteur types of strains to create a wild type phenotype. The commenter stated that combination of these two strains can be accomplished no matter what sort of physical security may be employed to prevent access, theft, loss, or release of the agent. The commenter concluded that more effective preventive measures can be achieved through training and educating microbiologists on how to avoid accidentally combining these two strains and by penalizing any individuals who intentionally try to combine them.

We agree with the commenters that *Bacillus anthracis* Pasteur strain is attenuated and poses a significantly lower risk than wild type *Bacillus anthracis* strains. We also agree that the Pasteur strain is not likely to have the potential for mass casualties or devastating effects to the economy, critical infrastructure, or public confidence and therefore does not meet the criteria used to apply the Tier 1 designation. In addition, we note that the Pasteur strain has been used successfully as a veterinary and human vaccine, which further demonstrates the attenuation of this strain. Therefore we have determined that the *Bacillus anthracis* Pasteur strain should not be designated as a Tier 1 select agent.

While we agree that the *Bacillus anthracis* Pasteur strain does not meet the criteria for inclusion as a Tier 1 select agent, we do not agree with the argument that regulating the *Bacillus anthracis* Pasteur strain would not serve to prevent the accidental (or intentional) generation of a wild type *Bacillus anthracis* strain by the combination of the *Bacillus anthracis* Pasteur strain with the *Bacillus anthracis* pXO1+/ pXO2- Sterne strain. Retaining the

*Bacillus anthracis* Pasteur strain as a select agent will allow for continued oversight of laboratories in which the accidental (or intentional) combination of this strain with the *Bacillus anthracis* Sterne strain could occur to produce the wild type phenotype of *Bacillus anthracis* de novo. Failure to retain the *Bacillus anthracis* Pasteur strain as a select agent could result in an environment in which the probability of creation of virulent wild type *Bacillus anthracis* strains by the combination of non-regulated strains would be enhanced. Therefore, we have chosen not to exclude the *Bacillus anthracis* Pasteur strain from the list of select agents in this rulemaking. We will continue to evaluate exclusion requests as additional information becomes available in this area.

As explained above under the heading ''VS Select Agents and Toxins,'' avian influenza virus (highly pathogenic) is currently on the list of VS only select agents and toxins. One commenter recommended that, in light of recent studies whereby researchers have generated derivatives of influenza virus A (H5N1) capable of efficient aerosol transmission, we add ''Replication competent forms of influenza virus A (H5N1) capable of efficient aerosol transmission in ferrets or primates containing any portion of the coding regions of all eight gene segments [influenza virus A (H5N1) capable of efficient aerosol transmission in ferrets or primates]'' to the list of overlap select agents and toxins. The commenter also recommended that this type of avian influenza virus be classified as a Tier 1 agent given the historical 50 percent case-fatality rate of avian influenza virus A (H5N1) in humans.

The select agent program is currently in discussions regarding this issue and may address it in future rulemaking. Given the stage these discussions are in, however, we are not making any changes in this final rule based on this comment.

**Reorganization of the Current List of Select Agents and Toxins**

We proposed to establish a number of select agents and toxins as ''Tier 1'' select agents and toxins within the lists of VS and overlap select agents and toxins. Specifically, we proposed to list foot-and-mouth disease (FMD) virus and rinderpest virus as Tier 1 VS select agents and toxins and *Bacillus anthracis, Burkholderia mallei,* and *Burkholderia pseudomallei* as Tier 1 overlap select agents and toxins. We did not include PPQ select agents and toxins in this proposed reorganization because none of the PPQ select agents and toxins met the minimum criteria for inclusion on the proposed Tier 1 select agents and toxins list. All other select agents and toxins would continue to be subject to the current requirements concerning select agents and toxins.

One commenter argued that *Burkholderia mallei* and *Burkholderia pseudomallei* should not be classified as Tier 1 select agents. The commenter stated that these two select agents do not represent the same level of concern as the other select agents proposed for inclusion in Tier 1 and should therefore be assigned non-Tier 1 status.

Another commenter observed that *Bacillus anthracis* is less virulent than either *Yersinia pestis* or *Francisella tularensis*, which are on the list of HHS only select agents and toxins. The commenter additionally stated that the virulence of all three is far less than that of the hemorrhagic fever viruses and the encephalitis viruses that were not proposed for inclusion on the list of Tier 1 select agents and toxins. The commenter stated that significant advances have been made in the development of products for environmental decontamination and prophylaxis against inhalation of *Bacillus anthracis.*

We are making no changes to the regulations as a result of these comments. The process by which we determined which select agents and toxins should be designated as Tier 1 was multi-faceted and we are confident in the results of that process. Our determinations were not based on one aspect of each of the proposed select agents or toxins only. In order to determine which select agents and toxins should be given Tier 1 status, a two-part risk analysis was conducted on each. First, experts in the biology of these agents and toxins evaluated their potential for mass casualties or devastating effects to the economy, critical infrastructure, or public confidence. This process included assessments of morbidity and mortality, communicability, low infectious dose, availability of countermeasures, and economic impact of a potential attack. Second, each select agent and toxin was assessed for its risk of deliberate misuse, including its history of weaponization and/or known interest by State or non-State adversaries. These evaluations, combined with input from public comments received on our July 2010 ANPR and relevant findings in recent government and non-government reports, formed the basis for deliberations on which agents should constitute the Tier list. Agents that scored highly on both the public health and biothreat sets of criteria were judged to be those that were appropriately given a Tier 1 designation.

Two commenters pointed out that the categorization of select agents and toxins has already been carefully stratified into four biological safety levels (BSL) as specified by the CDC, with each BSL based on infectivity, virulence, and ease of transmission of the material in question. The commenters further observed that the Tier 1 designation implies the existence of a Tier 2 category which would require less attention to security. The commenters concluded that the process of tiering will only add confusion and administrative and financial burden to the current BSL grouping of select agents and toxins.

Two additional commenters stated that the proposed rule did not do enough to reduce the regulatory burden associated with non-Tier 1 agents. The commenters said that reduced levels of security requirements for personnel and facilities should be considered for non-Tier 1 agents.

In designating certain select agents and toxins as ''Tier 1,'' the select agent program considered and rejected the idea of designating the remaining select agents and toxins as ''Tier 2.'' The aim of establishing the Tier 1 category is to account for and respond to the particular risks associated with the agents and toxins in this category by increasing their handling and security requirements accordingly. The establishment of the Tier 1 category is in no way intended to imply that the non-Tier 1 select agents and toxins pose a lesser risk to public health and safety than they have previously. In accordance with that fact, we have not decreased the handling and security requirements for those non-Tier 1 agents. Biosafety levels describe the required combination of lab practices and techniques, safety equipment, and lab facilities appropriate for the operations being performed using potentially harmful materials such as select agents and toxins while the Tier 1 designation institutes security measures applicable to the agents and toxins themselves. For this reason there is no conflict that exists between BSL classifications and Tier 1 select agents and toxins.

Two commenters expressed concern regarding the proposal to list rinderpest virus as a Tier 1 agent, given that there are already special conditions in place as contained in §§ 121.3(f)(3)(i), 121.5(a)(3)(i), and 121.9(c)(1) concerning its handling and tracking. The commenters suggested that an alternative approach would be for APHIS to designate rinderpest virus as

a pathogen with very special handling requirements that is not considered to be part of either category of select agents. The commenters argued that this approach is justified due to the fact that rinderpest has now been officially eradicated worldwide.

We disagree with the commenters' suggestion to classify rinderpest virus as a separate type of agent apart from either of the select agent categories of designation. While it is true that rinderpest was declared to be officially eradicated by the OIE on May 25, 2011, this development does not render the disease any less of a concern as a select agent with potential for misuse. Enacting the suggestion that rinderpest virus be treated as a pathogen with ''very special handling requirements'' and not as either a Tier 1 or non-Tier 1 select agent would only serve to create a further level of required administrative oversight for regulated entities.

One commenter stated that the proposed tiering system poses significant questions as to the nature of the risk assessment process. Specifically, the commenter questioned listing as Tier 1 agents bacterial diseases that are treated with licensed antibiotics, that are not commonly spread person to person, and that are present in the environment of the United States, while viruses that have no known therapy and that pose extreme risk to Western populations are absent. The commenter further stated that the 20 criteria used for evaluation of each select agent and toxin should be made available to the regulated community for review and assessment.

We are making no changes as a result of this comment. The relative ease by which exposure to a select agent or toxin may be treated is only one aspect considered by the select agent program when determining the tier status of each. The 20 criteria referenced by the commenter are those employed by the Federal Experts Security Advisory Panel (FESAP) in providing recommendations to the select agent program. The criteria that the FESAP used in its risk assessment process are:

1. The relative ease with which a select agent or toxin might be acquired from a laboratory or commercial source;
2. The relative ease of production of a select agent or toxin;
3. The relative ease by which a select agent or toxin might be modified in order to enhance its pathogenicity, transmissibility, or ability to evade medical and non-medical countermeasures;
4. The potential for easy deliberate dissemination;
5. The potential for creating disease or illness;
6. The relative environmental stability of a select agent or toxin by itself and how well it survives in the environment in which it is formulated or disseminated;
7. The amount of select agent or toxin necessary to induce illness;
8. The relative ease with which a particular select agent or toxin might be disseminated or transmitted from one animal or person to another or into the environment where it could produce a deleterious effect upon animal, plant, or human health;
9. Whether the target population has innate immunity to the select agent or toxin or whether immunity has been acquired from a source such as vaccines;
10. The potential for the select agent or toxin to create morbidity (i.e., any non-fatal illness that renders partial dysfunction to an animal or human lasting weeks or months that will eventually resolve with medical, veterinary, and/or supportive care);
11. The burden placed on the human, veterinary, or plant health system by the deliberate release of the select agent or toxin;
12. The ability to detect a release of the select agent or toxin into the environment, food, water, or soil;
13. The ability of the human and agricultural health authorities to accurately and rapidly diagnose and treat the disease presented by a release of the select agent or toxin;
14. The existence of countermeasures to prevent, treat, or mitigate the symptoms of a disease caused by the release of a select agent or toxin and/or its spread through a population;
15. The potential for high animal, plant, or human mortality rates with delivery of medical countermeasures;
16. The potential for high animal, plant, or human mortality rates without delivery of medical countermeasures;
17. The short-term economic impact of a single outbreak of a disease or release of a toxin;
18. The human, monetary, and other resource costs of making an area, building, industrial plant, farm, or field safe for humans, animals or plants to inhabit following the release of the select agent or toxin;
19. The pathogen's ability to persist in the environment or to find a reservoir that makes its recurrence more likely; and
20. The long-term health or economic consequences caused by a single release of the select agent or toxin.

We believe that the process by which determinations were made regarding the Tier 1 or non-Tier 1 status of the select agents and toxins was responsive to regulated community concerns received during the comment period for the advance notice of proposed rulemaking as well as for the proposed rule.

One commenter asked why the requirements for working with plant pathogens had not been lessened. The commenter stated that a transparent process does not exist that is inclusive of expert opinion from both the private and public sectors to determine which agents should be removed or added to the list of select agents and toxins.

We are making no changes as a result of this comment. In creating the Tier 1 class of agents, the Select Agent Program considered and rejected the idea of designating the remaining agents as ''Tier 2.'' The aim of establishing the Tier 1 category is to account for and respond to the particular risks associated with the agents and toxins in this category by increasing their handling and security requirements accordingly. The establishment of the Tier 1 category is in no way intended to imply that the non-Tier 1 agents pose a lesser risk to public health and safety than they have previously. In accordance with that fact, we have not decreased the handling and security requirements for those non-Tier 1 agents. Further, we determined that the establishment of more varying levels of risk would serve to create the need for increased administrative oversight and complication for regulated entities. We believe that the process by which these determinations were made was sensitive to public and expert opinion via the comment period on the initial advance notice of proposed rulemaking as well as on the proposed rule.

Security Measures for Tier 1 Select Agents or Toxins

We also proposed additions to the VS regulations that would allow for the optimization of security measures for those select agents or toxins that are designated as Tier 1. These requirements included:

- Additions regarding the assessment of persons prior to their access to Tier 1 select agents and toxins that would be made to the security plan currently required to be developed by all entities seeking approval for the possession, use, and transfer of select agents and toxins; ongoing oversight of those persons with access to Tier 1 select agents and toxins; and the role of the entity's responsible official in coordinating and assuring the security of Tier 1 select agents and toxins;
- Security enhancements that include provisions for security barriers, intrusion detection and monitoring,

delay/response force, access control, and information security;

• Additions to the biosafety plan currently required to be developed by all entities seeking approval for the possession, use, and transfer of select agents and toxins that would describe implementation of an occupational health program for individuals with access to Tier 1 select agents and toxins;

• Development of security policies and procedures describing the entity's response to a failure of an intrusion detection or alarm system and notification procedures for the Federal Bureau of Investigation (FBI) in the event of theft or suspicious activity that may be criminal in nature involving a Tier 1 select agent or toxin. These policies and procedures would be required as part of the entity's incident response plan; and

• Required annual insider threat awareness briefings focused on how to identify and report suspicious behaviors.

We have made changes to some of these proposed requirements, which are discussed in detail below.

Many commenters had questions or concerns regarding the additions to the security plan for those entities possessing a Tier 1 select agent or toxin as proposed in 9 CFR 121.11(e). Specific issues addressed by the commenters included: Conduct of pre-access suitability assessments, ongoing suitability assessments, and 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. Commenters generally fell into two categories in their responses to the proposed additions: Some felt that the requirements were too vague to prove useful, creating administrative burden without improving the overall security of Tier 1 select agents and toxins, while others felt that the requirements could or would require entities to behave in a manner contrary to local laws, privacy laws, or union contracts.

For the most part, we anticipate that these requirements are already being met and that these regulations will merely require those entities possessing a Tier 1 select agent or toxin to codify and document the systems and processes currently in place. It should be noted that many of the specific concerns raised by commenters regarding potential violation of laws or union contracts arose as a result of the commenters' examination of those recommendations given to the select agent program by the FESAP. As a matter of clarification, the select agent program considered the FESAP recommendations, as well as recommendations from other sources (e.g., *National Science Advisory Board for Biosecurity*), in developing the proposed rule and suitability assessment guidance documents; however, we are not adopting all of the specific recommendations found in these studies. While we have created specific guidance to aid in compliance with this section of the revised regulations, we are deliberately leaving the regulatory text in its broadly-written state in order to allow entities a measure of flexibility in how they meet the requirements. Given our experience with the select agent and toxin regulations and the wide variety of regulated entities the regulations cover, we have found this to be the most effective approach. The guidance document developed in conjunction with this rule is, in part, a response to the questions and issues raised by the commenters. Issues addressed in this document include, but are not limited to:

• Understanding the risks and reasons for suitability assessments;

• Delineating the roles and responsibilities of individuals to ensure optimal security;

• Requesting information about individuals in a standardized manner and assessing individuals in the context of safety and security;

• Responding to reports in a consistent, prompt, and confidential manner; and

• Providing training for recognizing and reporting suspicious behavior.

Full guidance on this and other issues may be found on the National Select Agent Registry at *www.selectagents.gov*.

In 9 CFR 121.11(e)(4)(i), we proposed that regulated entities with Tier 1 select agents and toxins prescribe and/or implement ''procedures that 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, the protection of animal or plant health and animal or plant products, security, and the integrity of the scientific enterprise.'' We are making a minor change to the proposed language in 9 CFR 121.11(e)(4) in order to stipulate that entities must implement these security enhancements, not merely prescribe and/or implement them. The proposed rule stated that ''Entities with Tier 1 select agents and toxins must prescribe and/or implement the following security enhancements.'' We are removing the words ''prescribe and/or'' for the purposes of clarity. Our original intent in creating that provision was to require the use of the security enhancements in question by those entities with Tier 1 select agents or toxins. By removing the words ''prescribe and/or'' we are eliminating a potential loophole by which entities may have been able to establish but not fulfill these requirements while remaining in compliance with the regulations.

Regarding the proposed language in 9 CFR 121.11(e)(4)(i), one commenter stated that the use of the phrase ''trustworthy and behaving in a manner that upholds public health and safety, the protection of animal or plant health and animal or plant products, security, and the integrity of the scientific enterprise'' would establish a regulatory standard that would prove difficult or impossible to enforce due to its subjective nature.

We agree with the commenter's observation and have changed the language to require that entities possessing Tier 1 select agents or toxins prescribe and implement ''procedures that will limit access to a Tier 1 select agent or toxin to only those individuals who are approved by the HHS Secretary or Administrator, following a security risk assessment by the Attorney General, have had an entity-conducted pre-access suitability assessment, and are subject to the entity's procedures for ongoing suitability assessment.'' We believe that this establishes a more specific set of requirements for regulated entities.

In 9 CFR 121.11(e)(4)(iv) we proposed that regulated entities with Tier 1 select agents and toxins establish 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 would be required to 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.) Two commenters requested clarification regarding what was meant by the term ''barrier'' and asked for examples of what constitutes a barrier. The commenters suggested that a definition for ''barrier'' be added to the definitions sections in 7 CFR 331.1 and 9 CFR 121.1.

We agree with the commenters and we have added a definition for *security barrier* to read as follows: ''A physical structure that is designed to prevent entry by unauthorized persons, animals, or materials.'' In addition, we have altered the language concerning security

barriers in 9 CFR 121.11(f)(4)(iv) in order to clearly indicate that the final security barrier must limit access to the select agent or toxin to personnel approved by the HHS Secretary or Administrator and following a security risk assessment by the Attorney General.

In 9 CFR 121.11(e)(4)(v), we proposed that all registered space and areas that reasonably afford access to the registered space must be protected by an intrusion detection system (IDS) unless physically occupied. One commenter stated that the proposed requirement contained a potential loophole by which an entity could argue that the presence of a janitor or similar personnel in registered space outside of normal working hours would allow that entity to avoid installation of an IDS. The commenter suggested that such a situation could be avoided by adding a stipulation that an IDS would need to be used when the entity was not ''physically occupied by the routine contingent of working, approved employees.''

We disagree with the commenter's observation as it is unlikely that the entity would be occupied at all hours, thus creating the loophole that would allow an entity to fail to install an IDS. We are also not adopting the commenter's suggestion to add language regarding the presence of approved employees as we believe that would create confusion concerning the number of employees that could be described as ''the routine contingent.'' Further, the IDS is one aspect of the security measures required for regulated entities. In the scenario proposed by the commenter, the IDS would not be engaged if a janitor or other personnel were present in the entity outside of normal working hours; however, the other required physical security measures would serve to protect the entity at that time. Finally, the training and employee suitability assessments required for those employees with access to select agents and toxins would also serve to ensure that those employees who work in registered areas understand and can employ the necessary security and safeguarding measures to maintain the physical security of the entity.

In 9 CFR 121.11(e)(4)(vii), we proposed to require that entities provide backup power and energy sources to ensure that information security networks and integrated access controls and related systems will maintain power during emergencies. While we did not receive any comments on this issue, in response to comments received by CDC and in the interests of maintaining parity between the APHIS and HHS regulations, we are amending the text to stipulate that only those entities with powered access control systems will need to fulfill this requirement. We have also reworded the requirement to clarify that the aim is maintenance of physical security standards in the case of a power disruption and that this maintenance may, among the alternatives, take the form of backup power.

In 9 CFR 121.11(e)(4)(viii) we proposed that 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 for any entity with Tier 1 select agents and toxins. One commenter stated that such a requirement would be burdensome, unattainable, and cost-prohibitive depending upon the number and nature of the alarms. The commenter went on to state that the security system at their entity sounds an alarm when a door is held open longer than a preset length of time and that most alarms occur during working hours, primarily as the result of staff holding the door open too long. The commenter explained that requiring security respond to all these alarms is unwarranted, excessive, and costly. The commenter suggested that a better alternative would be for a laboratory supervisor or manager to be notified of and investigate these incidents, therefore allowing entities to respond in a manner commensurate with the severity of the incident that triggered the alarm.

Our selection of the 15 minute response time is based on Department of Defense (DOD) and DHS standards for high value assets and also on our analysis of incident response plans provided by the regulated community since 2003. However, based on this comment and others received by CDC, we have modified the language in this section. We have retained the 15 minute response time goal for security forces or local police, but we have also provided additional flexibility for entities to develop systems in line with the optimal achievable response time in their area. Entities may either incorporate the 15 minute response time into their security plans or determine an alternate response time calculated in conjunction with security forces or local police. Response time can be determined many ways. For example, an entity can:

- Enter into a formal agreement with local law enforcement.
- Discuss with local law enforcement.
- Discuss with the IDS service provider.
- Conduct an exercise with the guard force.

The issue of multiple false alarms and the potential costs associated with such a situation as raised by the commenter is more appropriately addressed at the entity level.

In 9 CFR 121.11(e)(4)(ix) we proposed to require that entities conduct complete inventory audits of all Tier 1 select agents and toxins in long-term storage 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, upon the departure or arrival of a principal investigator for those Tier 1 select agents or toxins under the control of that principal investigator, or in the event of a theft or loss of a Tier 1 select agent or toxin.

We have reevaluated this provision in light of comments received on the CDC rule and, based on our experience with the select agent program, we believe that this requirement needs to be applied to all select agents and toxins, and not only Tier 1 select agents and toxins. This change serves to codify our current policy concerning inventory audits. We have therefore revised the language to address inventory verification for all select agents and toxins.

In the case of those entities which possess FMD and rinderpest virus, we proposed to require four barriers, including one barrier that is a perimeter security fence or equivalent. These requirements were listed in proposed 9 CFR 121.11(e)(5)(i). One commenter inquired as to what the equivalent to a perimeter security fence would be. The commenter also wished to know if an IDS would be considered a barrier.

One equivalent to a perimeter security fence would be a perimeter wall surrounding a specific building, complex, compound, or campus, with 24 hour a day, 7 days a week monitoring. Such a wall would serve a purpose identical to a perimeter security fence. We have developed guidance to assist entities with the security barrier requirement, which covers the issue of perimeter fencing. Guidance documents may be found on National Select Agent Registry at *www.selectagents.gov.* As to the commenter's question regarding the IDS: As stated above, a security barrier would include only natural or man-made obstacles preventing or delaying the movement of persons, animals, or materials. While an IDS may alert security or other personnel to potential incidents, the IDS itself would not be considered to be a security barrier since it does not actively create an obstacle or delay.

Another commenter asked whether the proposed requirements would make it illegal for U.S. veterinary diagnostic

laboratories to perform diagnostic and/or surveillance testing following an FMD outbreak on U.S. soil if the laboratories in question did not have a fourth security barrier. The commenter recommended that we revise the paragraph in order to clarify our intent.

We are making no changes as a result of this comment. The select agent program recognizes the critical role of diagnostic laboratories in the early detection of and response to outbreaks of select agent and toxin-related disease in humans and agriculture. While all of the Tier 1 regulatory requirements will apply to entities that maintain permanent stocks of Tier 1 select agents and toxins, in the case of a public health or agricultural emergency, a diagnostic laboratory may request to retain the select agent or toxin under the provisions contained in 9 CFR 121.6(e).

Two commenters recommended that the select agent program consult with administrators and laboratory managers from public and private research institutions prior to the development of any framework of suitability that can be used to address security concerns.

We will engage subject matter experts as necessary in the development of guidance documents which may be found on the National Select Agent Registry at *www.selectagents.gov*. The select agent program welcomes feedback on the usability and usefulness of existing guidance documents at any time.

One commenter suggested that the minimum security provisions for Tier 1 select agents and toxins should include video monitoring of all select agents and toxins work and storage areas, a two-person rule for entry into select agents and toxins work and storage areas, and psychological assessment and monitoring of those employees working with select agents and toxins.

We are making no changes as a result of this comment. The specific measures the commenter suggested were considered and rejected in favor of the more general requirements listed. The select agent program is highly conscious of the need to balance biosecurity and biocontainment concerns with allowing entities the necessary flexibility so as to not impede their research unduly. Since there is variety in the type and size of entities covered under the regulations, we believe this approach is warranted. We would note that the regulations do not preclude any given entity from adopting the approach suggested by the commenter, among others.

One commenter stated that, while many of the proposed security changes are already in place, some are not and it was unclear that additional costly or impractical security measures would provide any additional benefit since existing measures have proven adequate to protect the security of these agents.

We are making no changes as a result of this comment. It was our determination, based on the information available to us, that the additional security requirements would not constitute an economic burden on the regulated entities. In many cases these regulations serve to codify systems and procedures already in use in these regulated entities.

The regulations in 9 CFR 121.12 concern the development of a biosafety plan that establishes measures sufficient to contain the select agent or toxin (e.g., physical structure and features of the entity, and operational and procedural safeguards). We proposed to add a paragraph that would stipulate that entities registered to possess Tier 1 select agents or toxins establish an occupational health program for individuals with access to Tier 1 select agents and toxins. One commenter recommended that the occupational health program requirements be instituted for all select agents and toxins, regardless of their categorization.

We are making no changes in response to this comment. Due to the greater level of concern associated with Tier 1 select agents and toxins the select agent program needs to ensure that entity safety protocols are in place. Further, after considering the issue and in light of the fact that it caused confusion amongst some commenters on the CDC proposed rule, we are eliminating the sentence that reads, ''The occupational health program may also be made available to individuals without access to Tier 1 select agents and toxins.'' While we believe that regulated entities should use their discretion and judgment in considering whether the creation of an occupational health program applicable to those employees working with non-Tier 1 select agents and toxins is needed, such a suggestion is not appropriately contained in the regulations. Guidance on the development of an occupational health program may be found on the National Select Agent Registry at *www.selectagents.gov.*

The regulations in 9 CFR 121.15 concern required mandatory training for staff and visitors who work in or visit areas where select agents or toxins are handled or stored. In 9 CFR 121.15(b), we proposed to add a requirement that entities with Tier 1 select agents and toxins must conduct annual insider threat awareness briefings on how to identify and report suspicious behaviors. One commenter stated that this training should be required for all registered entities possessing, storing, or transferring select agents, not just those with Tier 1 select agents or toxins.

We are making no changes in response to this comment. Due to the greater level of concern associated with Tier 1 select agents and toxins the select agent program needs to ensure that entity safety protocols are in place. Regulated entities should use their discretion and judgment in considering whether the creation of an annual insider threat awareness training program applicable to those employees working with non-Tier 1 select agents and toxins is needed. Guidance on the development of annual insider threat awareness training may be found on the National Select Agent Registry at *www.selectagents.gov.*

Another commenter asked for clarification and guidance regarding the requirement for annual insider threat awareness briefings. The commenter asked that the content of these threat awareness briefings be made available to public health laboratories so that it could then be specifically customized for various regions of the country.

While we have created specific guidance regarding this section of the revised regulations, that guidance does not take the form of a prescriptive program with content that may then be adapted and distributed as the commenter requests. Given our experience with the select agent and toxin regulations and the wide variety of regulated entities those regulations cover, we have found a broader approach to be most effective. The guidance documents developed in conjunction with this rule are, in part, a response to the questions and issues raised by the commenters. The documents will contain specific examples of best practices that we believe entities would be well served in adopting including, but not limited to, a designated person to manage the assessment of laboratory personnel, laboratorian involvement in threat migration, and those behaviors of concern which may indicate a possible insider threat. Full guidance on this and other issues may be found on the National Select Agent Registry at *www.selectagents.gov.*

**Miscellaneous Changes**

We proposed to make several smaller-scale changes to the regulations, including the addition of definitions and clarification of language concerning security, training, biosafety, biocontainment, and incident response. These changes are intended to increase the usability of the select agent

regulations as well as provide for enhanced program oversight.

In 7 CFR 331.1 and 9 CFR 121.1, we proposed to add definitions for *adjudicated as a mental defective, alien, committed to any mental institution, controlled substance, crime punishable by imprisonment for a term exceeding 1 year, indictment, lawfully admitted for permanent residence, mental institution,* and *unlawful user of any controlled substance.* These definitions, which described specific aspects of the proposed definition of *restricted person,* were intended to assist regulated entities 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.

Four commenters stated that these definitions needed to be further clarified. The commenters generally characterized the proposed definitions as either overly restrictive or vague. After careful consideration we have agreed with the commenters and have decided not to include these definitions or a definition for *restricted person* in the final rule. We will look to develop additional guidance in this area.

We proposed to add a definition for *recombinant and synthetic nucleic acids.* This addition was deemed necessary, as the term ''synthetic nucleic acids'' is employed in the proposed changes to the select agent regulations. We proposed to include synthetic nucleic acids in the regulations because, while synthetic nucleic acids have the same potential for harm as recombinant nucleic acids, the process of production is different.

One commenter stated that the proposed definition has implications in all areas currently impacted by synthetic biology technology, such as industrial enzymes, renewable chemicals for pharmaceutical and industrial applications, bio-based products, personal care products, renewable specialty chemicals, biofuels, and healthcare products. The commenter argued that consequences of adopting the proposed definition could impede the growth of sustainable products from emerging fields such as synthetic biology technology. The commenter therefore recommended that we not adopt the new definition of *recombinant and synthetic nucleic acids* as stated in the proposed rule, arguing that the existing language of the regulation is sufficient to cover the current uses of synthetic nucleic acids. The commenter further stated that the proposed definition utilizes language that was proposed to, but rejected by, the National Institutes of Health Recombinant DNA Advisory Committee (NIH–RAC). The commenter suggested that if the select agent program finds it necessary to introduce a new definition for *recombinant and synthetic nucleic acids,* that we follow the leadership of the NIH–RAC and establish a simpler definition that is not focused on the underlying mechanism of production of the nucleic acids.

We disagree with the commenter's assertion regarding the broad impact of the definitions used by the select agent program. Our scope of oversight is limited to the list of select agents and toxins and therefore does not extend to all synthetic biology. However, we do agree that any definition adopted for use in the regulations should be based on the most current information available from subject matter experts. Following extensive consultation with the NIH, we have updated the definition of *recombinant and synthetic nucleic acids* to reflect the most current thinking on the subject. In addition, we have separated the definition of *recombinant nucleic acids* from the definition of *synthetic nucleic acids* for purposes of clarity.

We proposed to add a definition for *occupational exposure* to the VS regulations in 9 CFR 121.1 as it is used in the regulations but not defined. This definition was based on that used in the Occupational Safety and Health Administration regulations in 29 CFR 1910.1030. We did not propose to add a corresponding definition to the PPQ regulations in 7 CFR 331.1 since PPQ select agents and toxins do not pose a severe threat to human health and, therefore, it is unnecessary to address personnel safety and health. One commenter suggested that we expand the definition to specify that, due to aerosol transmission, such exposure incidents may impact other employees working in the same area.

We agree with the commenter that the proposed definition did not adequately address the possibility of aerosol transmission and have amended the language accordingly.

Additionally, we are also removing references to rickettsiae in the definitions for *biological agent* and *toxin.* This change is necessary because there are no rickettsiae select agents or toxins regulated by APHIS on the list of select agents and toxins.

We proposed to amend 7 CFR 331.3(e), 9 CFR 121.3(e) and 9 CFR 121.4(e). These paragraphs specify that attenuated strains of select agents or toxins may be excluded from the requirements of the select agent regulations subject to an official request and supporting scientific information. We proposed to state that the ''inactive form of a select toxin'' may be excluded from regulation under each respective part subject to the application procedure. We also proposed to update the Web site address in paragraph (e)(1) of each section as all information concerning the Select Agent Program is now centralized on the National Select Agent Registry at *http://www.selectagents.gov/*. Finally, we proposed to remove the language stating that exclusions will be published in the **Federal Register**. At the time the regulations were initially created we anticipated publication of exclusions both in the **Federal Register** and on the Internet; however, we have found that publication on the National Select Agent Registry Web site only has served to provide the most up-to-date information to the regulated community.

One commenter suggested that, in addition to publication of exclusions on the National Select Agent Registry Web site we should also develop and maintain an email distribution list so that registered facilities could be notified when updates are added to the Web site.

We currently engage in the type of email updates that the commenter suggests. Emails are sent to responsible officials and alternate responsible officials at all registered entities. Dissemination of that information is at the discretion of the responsible officials and alternate responsible officials. We plan on issuing guidance and suggestions regarding information dissemination, which we believe will enable further information sharing within regulated entities.

Another commenter asked that we add a timeline to the regulations indicating when the person requesting the exclusion should expect to receive a written response. The commenter stated that, in the case of grant applications, it may be difficult to meet deadlines if the applicant has no idea how long a response from the select agent program will take.

We are making no changes as a result of this comment. Due to the wide variety of material submitted for consideration for exclusions, establishment of a timeline as the commenter recommends is impractical. The select agent program necessarily examines each application on a case-by-case basis. We strive to make the process as efficient as possible.

The regulations in 9 CFR 121.6 set out guidelines for those instances where overlap select agents and toxins may be considered exempt from the regulations. Specifically, § 121.6(e) concerns

procedures by which an individual or entity may be exempted from the requirements of the regulations if necessary in order to respond to a domestic or foreign agricultural emergency involving an overlap select agent or toxin. Upon further consideration, in order to eliminate an unnecessary burden on such an individual or entity, we have removed the provision stating that the individual or entity must complete APHIS/CDC Form 5 in order to request such an exemption. Guidance on requesting an exemption for an individual or entity in the case of a domestic or foreign agricultural emergency involving an overlap select agent or toxin may be found on the National Select Agent Registry at www.selectagents.gov.

The regulations in 7 CFR 331.9 and 9 CFR 121.9 set out requirements for entities requesting to work with select agents and toxins to designate a responsible official, who ensures that the entity continues to meet the requirements of the regulations. We proposed to explicitly require that all designated responsible officials possess the appropriate training or expertise to execute their required duties. We also proposed 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. Finally, we proposed to add a requirement that the responsible official's principal duty station be the physical location of the registered entity.

One commenter stated that the language concerning responsible officials is not clear and may cause institutions to unnecessarily create new administrative structures and positions to meet this requirement. The commenter urged the select agent program to work with research institutions in order to identify the most appropriate level of administration for the responsible official.

We are making no change in response to this comment. The responsible official should be an individual who can perform all of the duties required for that position. The regulations were designed to place the responsibility for ensuring entity compliance with the regulations in one position. Given the wide variety of entities covered by the regulations, establishing more prescriptive guidelines would decrease the flexibility and usefulness of the regulations to those entities. We neither require nor prohibit the establishment of a separate administrative position for the responsible official as we leave it to the entity to decide how best to designate a responsible official who meets the requirements of the regulations.

Another commenter said that the absence of specific requirements regarding responsible official qualifications will establish an inspection process that is subjective and ineffectual. The commenter asked that we add a section that explains and/or defines what we consider the ''appropriate training or expertise'' necessary for an entity's responsible official.

We have established the regulations regarding the training and expertise of the responsible official in order that they provide maximum flexibility to regulated entities. The reasons for this are twofold: First, given the quickly developing and changing fields of biosafety and biosecurity, any attempt on our part to strictly define required training and expertise within the regulations would likely become obsolete as the parameters continue to evolve; second, given the wide variety of entities covered by the regulations, there is a need to maintain flexibility so that they may remain applicable to all of those entities. We have removed the reference to ''appropriate training or expertise'' and will continue to assess the performance of the responsible official based on his or her efficacy in implementing the regulatory requirements at his or her entity. With an eye to the non-specificity of the regulations, we have developed guidance documents regarding this and other aspects of entity compliance. They are available on the National Select Agent Registry at *www.selectagents.gov*.

Five commenters requested further clarification regarding the proposed requirement that the responsible official's principal duty station be the physical location of the registered entity. The commenters inquired whether this requirement would mean that the principal duty station should be in the same building or only at the same institution.

In response to these comments and others received by the CDC, we are modifying the language in 7 CFR 331.9 and 9 CFR 121.9 to stipulate that the responsible official must have a physical (as opposed to a telephonic or audio-visual link) presence at the registered entity to ensure that the entity is in compliance with the regulations. The responsible official will also be more quickly able to respond to any on-site incidents involving select agents and toxins if he or she is on-site.

Three commenters asked that the definition of ''entity'' be clarified in relation to the requirement that the responsible official's principal duty station be the physical location of the registered entity and the impact of the requirement assessed. The commenters' request was based on their understanding that an entity has to be contiguous and that laboratories separated on a campus constitute separate entities. The commenters concluded that having separate responsible officials in this case would be burdensome.

We realize that many entities are located on a campus with several registered laboratories in different buildings. The intent of this requirement is not to ensure that a responsible official is assigned to each physical laboratory but to ensure that the responsible official is physically located on the campus.

We proposed to amend the regulations in 7 CFR 331.10 and 9 CFR 121.10. These regulations establish parameters for restricting access to select agents and toxins and the process by which individuals may be approved for access to select agents and toxins after the completion of a security risk assessment by the Attorney General. Specifically, we proposed to add new provisions by which individuals may have access to select agents at entities other than the individual's ''home'' entity. We also proposed to decrease the maximum length of time for which a security risk assessment will be valid from 5 years to 3 years in order to more expeditiously identify individuals who may have fallen into one of the prohibited or restricted categories.

One commenter asked whether, during the time period in which an individual has access to select agents at entities other than the individual's ''home'' entity, that individual would have access to select agents at both facilities, or if the access approval would be transferred so that the individual would only have access to the select agents and toxins at the new entity for the time specified. The commenter stated that, from a biosafety and biosecurity perspective, limiting access to only one entity at the time would be appropriate.

During this timeframe, the individual will maintain access to select agents at both facilities. We believe that such an arrangement will serve to facilitate collaboration between registered entities as well as enabling various entities to use their time and funds most efficiently in order to continue ongoing research. We do not agree with the commenter's assertion that this procedure would threaten biosecurity or biosafety in any way since all registered entities are

required to undergo the same security screening process as established by the regulations.

Two commenters stated that decreasing the maximum length of time for which a security risk assessment will be valid from 5 years to 3 years would represent an undue burden on registered entities. One commenter cited the generally low rate of turnover at these entities, while the other stated that the existing policy, with renewal every 5 years, has proven to be both sufficient and cost effective since the establishment of the select agent regulations. The first commenter suggested that we allow for less frequent risk assessments in the case of those individuals working with non-Tier 1 select agents and toxins only. The second commenter recommended making no changes to the 5-year interval.

The decision to begin processing security risk assessments at 3-year rather than 5-year intervals was made as a result of the recommendations from a working group comprised, in part, of representatives from the DOD and the HHS as well as various subject matter experts. Based on input from the working group as well as the FBI, we have determined that conducting security risk assessment approvals every 3 years is an effective method for increasing the security of our entities. Furthermore, the select agent program has been processing security risk assessments on a 3-year basis since June 1, 2011. Since that date, we have not received any comments from the regulated community regarding additional financial or administrative burden associated with the changed practice. Regarding the first commenter's suggestion to process security risk assessments differently for those individuals working with non-Tier 1 select agents and toxins only, the establishment of the Tier 1 category is in no way intended to imply that the non-Tier 1 agents pose a lesser risk to public health and safety than they have previously. In accordance with that fact, we have not decreased the handling and security requirements for those non-Tier 1 agents.

We proposed to require that the security plan described in 7 CFR 331.11 and 9 CFR 121.11 that must be developed by all registered entities be submitted for initial registration, renewals of registration, and at any other time upon request to replace the existing requirement that they be provided upon request only. We also proposed that the security plan 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. We also proposed to add a requirement that the security plan include procedures that require the responsible official to immediately notify the FBI in order to initiate a threat assessment process in the event that he or she becomes aware of suspicious activity which is criminal in nature, related to the facility, its personnel, or select agents. We also proposed to add provisions for information security, including the need for backup measures if the entity relies on information systems for security. We also proposed 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. Finally, we proposed to amend paragraph (e) in 7 CFR 331.11 and 9 CFR 121.11, which previously directed individuals creating a security plan to guidance for developing such documents contained in the ''Morbidity and Mortality Weekly Report'' from December 2002. We proposed that applicants would instead be directed to the ''Security Information Document'' and the ''Security Plan Template'' on the National Select Agent Registry Web site.

Two commenters requested clarification concerning the proposed requirement that entities address procedures concerning animals or plants accidentally or intentionally exposed to or infected with a select agent. Specifically, the commenters requested clarification as to whether the requirement would be limited to experimental plants and animals that are possessed and controlled by the registered entity. One commenter suggested two additions to the requirements: One stipulating that the incident response plan only cover those animals or plants possessed and controlled by the entity and the second a certifying statement confirming that the State animal health official (or plant-associated equivalent) has an incident response plan in place to address intentional or accidental exposure to select agents for animals or plants throughout the State, including those plants or animals that are not possessed or controlled by the entity but may be located on the premises (e.g., wild animals).

We are making no changes based on these comments. It was always our intent that the entity's incident response plan be limited to those exposed plants and animals that are possessed by and controlled by the registered entity.

One commenter suggested that we alter the wording from a requirement to safeguard animals or plants ''intentionally or accidentally exposed to or infected with a select agent'' to a requirement to safeguard animals or plants ''intentionally exposed to, or infected with, select agents.'' The commenter stated that the suggested language would be clearer.

We are making no changes based on this comment. We believe that animals or plants accidentally exposed to or infected with a select agent should be handled as select agents and safeguarded in the same manner as an animal or plant intentionally exposed to a select agent.

In the preamble to the proposed rule, we stated that we were not proposing to require the security plan to address animals and plants exposed to select toxins. This is because recovering the toxin from within an animal or plant subject is highly difficult and such removal does not produce a reasonable yield of recovery. In addition, there is uncertainty as to whether or not the toxin would remain active when recovered from the animal or plant. For these reasons it is highly unlikely that once introduced into an animal or plant, a sufficient amount of toxin could be recovered to pose a significant hazard to public health, agriculture, or agriculture products. One commenter questioned that rationale, stating that while toxins are unlikely to be amplified or move into multiple hosts outside a given facility, there is still concern that amplification of toxins could occur in animals or insects during the course of an experiment.

We disagree with the commenter's assertion. Select toxins do not amplify the way select agents do. Toxins in an animal or insect would prove deadly to that organism before it could reach a level at which extraction would become possible.

One commenter stated that our proposal to add a requirement that the security plan include procedures for the responsible official to notify the FBI of suspicious activity that may be criminal in nature and related to the entity, its personnel, or its select agents or toxins contradicts guidance contained in the Nationwide Suspicious Activity Reporting (SAR) Initiative (NSI) established by the Department of Justice, creates a conflict within those entities that have their own recognized law enforcement agencies, and unnecessarily adds confusion due to the potential for concurrent jurisdiction. Two other commenters questioned the

rationale for requiring FBI reporting given that the select agent program is jointly administered by APHIS and CDC and, in the past, security concerns were directed to those agencies.

We do not believe that there exists any conflict between the security requirements in 7 CFR 331.11 and 9 CFR 121.11 and the guidance offered by the NSI. The intent of this requirement is to facilitate the involvement of antiterrorism resources which will increase the security of select agents and toxins. FBI field offices, which are centrally located in major metropolitan areas across the United States, can assist entities by working closely with them on crime threats. However, we agree with the commenters that it may be appropriate that notification of suspicious activity first be given to local law enforcement. We have therefore changed the language in 7 CFR 331.11(c)(8) and 9 CFR 121.11(c)(8) to read: ''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 describe procedures for how the entity will notify the appropriate Federal, State, or local law enforcement agencies of such activity.''

Another commenter suggested that we require FBI notification for any suspicious activity involving select agents or toxins and not just activity that may be criminal in nature. The commenter argued that it is more appropriate for the FBI to determine whether or not the activity in question is criminal in nature.

We are making no changes in response to this comment. The intent of this section of the regulations is to avoid excessive reporting to the FBI. It is our belief that a reasonable person would be able to determine if the behavior in question constitutes a potential criminal act, which would therefore necessitate FBI reporting.

One commenter requested that we provide further details concerning the proposed requirements for additions to the security plan, specifically as it relates to information security.

The purpose of the requirement in question is to clarify the language in 7 CFR 331.11(c)(9)(i) and 9 CFR 121.11(c)(9)(i) of the regulations that requires the entity to have procedures in place for information systems control. This is an overarching requirement that covers electronic and non-electronic information oversight by the regulated community. Our intent is not to regulate experimental data or the results of studies involving select agents and toxins but to regulate the select agents and toxins themselves. Therefore, we have revised the language in order to clearly indicate that the information security provisions in question should only be for access to the entity's registered space and records pertaining to select agents and toxins, as identified in sections 7 CFR 331.11, 9 CFR 121.11, 7 CFR 331.17, and 9 CFR 121.17.

Another commenter stated that the information security requirement represents an added regulatory burden, and the impact of this requirement should be evaluated.

For the most part, we anticipate that these requirements are already being met and will merely require entities to codify and document the systems and processes currently in place. The guidance documents developed in conjunction with this rule are, in part, a response to the questions and issues raised by the commenter. Issues addressed in this document include, but are not limited to: Information technology security, network security, computer security, peripheral devices and data storage, physical security and its application to information security, risk management, and training. Full guidance on information security may be found on the National Select Agent Registry at *www.selectagents.gov.*

Another commenter said that the proposed requirement that authorized and authenticated users only be 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 their access be modified when the user's roles and responsibilities change or when their access to select agents and toxins is suspended or revoked, would require registration and security risk assessments for all staff managing records pertaining to select agent work. The commenter argued that this requirement would increase the burden on manufacturers and institutions who utilize administrative or information technology staff for such document management.

The security requirements referenced by the commenter refer only to those persons who have either physical access to select agents and toxins or who have the capability to alter security access to select agents and toxins. Guidelines concerning security requirements such as these may be found on the National Select Agent Registry at *www.selectagents.gov.*

Another commenter stated that the meaning of the phrases ''network connectivity monitoring'' and ''backup security measures in the event that access control systems and/or surveillance devices are rendered inoperable'' should be clarified.

Again, we note that, further details regarding these and other aspects of the information security requirements may be found in the guidance documents mentioned above, which may be found on the National Select Agent Registry at *www.selectagents.gov.*

We proposed to require that an entity's security plan 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 would provide that an entity must properly secure containers on site and have a written contingency plan for unexpected shipments. One commenter requested clarification regarding the meaning of the term ''unexpected shipments.''

We believe that the term ''unexpected shipments'' is self-explanatory and believe that the security plan should contain procedures for these handling unexpected shipments (e.g., when an entity receives a shipment of a select agent that it had neither requested nor coordinated for, and therefore was not expecting).

The regulations in 7 CFR 331.13 and 9 CFR 121.13 concern restricted experiments, which are those experiments that may not be performed by regulated entities without the approval of the Administrator. In addition to the existing prohibition on conducting restricted experiments, we proposed to state that entities would not be authorized to possess the products of restricted experiments without the approval of the Administrator.

We also proposed to expand the restricted experiment approval requirement to include all experiments involving the creation of drug resistant select agents that are not known to acquire that resistance naturally, if such acquisition could compromise the use of the drug to control disease agents in humans, veterinary medicine, or agriculture, regardless of the method or technology used to create the resistance. Previously, the restricted experiment language concerned only those experiments involving recombinant DNA. We proposed this change because, while the introduction of a drug resistance trait would normally eliminate that drug as a therapeutic option to control the disease, there may be alternative drugs available to control the disease.

In addition, we are adding a reference to ''chemical resistance traits,'' to the PPQ regulations in 7 CFR 331.13 in order to capture the potential transfer of,

or selection for, such traits that could adversely affect plant and agricultural health. Chemical resistant traits include, but are not limited to herbicide resistance, fungicide resistance, and pesticide resistance. We did not propose to add a corresponding definition to the VS regulations in 9 CFR 121.13 since chemical resistance traits are exclusive to plant biology. It should be noted that restricted experiments are not prohibited experiments; an entity must seek permission prior to the initiation of a restricted experiment and receive approval from the Administrator or HHS Secretary. Approval for the performance of a restricted experiment or the possession of a product of a restricted experiment may involve meeting additional safety and/or security requirements as prescribed by the select agent program. Many experiments that involve the deliberate transfer of a drug resistant trait do not meet the definition of a restricted experiment because the drug is not used to control disease in humans, veterinary medicine, or agriculture. The select agent program encourages anyone who intends to conduct a select agent experiment utilizing drug resistance markers to submit that experiment for review so that they may be advised regarding whether the experiment would be considered a restricted experiment and therefore require approval prior to its initiation.

Two commenters were concerned about the proposed revisions classifying those experiments that introduce drug resistance to a select agent as restricted. The commenters suggested aligning the language concerning restricted experiments with the recombinant DNA guidelines issued by the NIH, which restrict and require approval only for those experiments with pathogens involving drug resistance for therapeutically useful agents against that pathogen. The commenters stated that the proposed language was too broad.

We made no changes as a result of these comments. Contrary to the commenters' assertion, we have not expanded the definition of a restricted experiment to include all experiments utilizing select agents or toxins with drug resistant traits, but only to those utilizing select agents or toxins with resistance to those drugs used to control disease in humans, veterinary medicine, or agriculture. The definition of a restricted experiment contained in the regulations is already aligned with the NIH recombinant DNA guidelines.

One commenter argued that antibiotic resistance not previously present could emerge in one or more select agents at any time. The commenter wished to know if the possession of such a previously unknown antibiotic resistant select agent would mean that all such organisms would be required to be destroyed. The commenter expressed concern that such a requirement might inadvertently prevent research in the case of a select agent that suddenly developed new antibiotic resistance traits.

We are making no changes to the regulations as a result of this comment. Regardless of whether the select agent develops a new trait, it is still considered and treated as a select agent from a biosafety or biocontainment perspective. The aspect of the process that makes a select agent the subject of a restricted experiment is the purposeful generation of antibiotic resistant properties. If a select agent developed new antibiotic resistance spontaneously, then it would be included in the category of select agents considered ''known to acquire the resistance naturally'' as specified in 7 CFR 331.13(a)(1) and 9 CFR 121.13(b)(1).

Another commenter wanted to know whether the use of the terms ''the select agent program'' and ''the Administrator,'' which refer to two different entities, indicates that restricted experiments would require the approval of both the select agent program and the Administrator.

Terms in this context are interchangeable, as the APHIS Administrator has delegated authority for establishing and enforcing the regulations to the select agent program. Approval is therefore only needed from the select agent program.

Another commenter stated that an ombudsman, in the form of additional working groups, should be included in the approval process for restricted experiments. The commenter said that involvement of such groups in this capacity would serve to engage those regulated scientists while furthering their understanding of the select agent program.

We are making no changes as a result of this comment. In reviewing applications to conduct restricted experiments, the select agent program utilizes the expertise of the Intragovernmental Select Agents and Toxins Technical Advisory Committee (ISATTAC), which is composed of Federal scientists from the CDC, NIH, FDA, APHIS, the Agricultural Research Service (ARS), APHIS' Center for Veterinary Biologics (CVB), and DOD, and its USDA counterpart, the Agricultural ISATTAC, which is composed of Federal scientists from ARS, APHIS, and CVB. In the past, when appropriate, we have engaged the advice of subject matter experts from outside the government.

The regulations in 7 CFR 331.14 and 9 CFR 121.14 concern development of an entity's incident response plan. We proposed to specify that each incident response plan be based upon a site-specific risk assessment. We also proposed that the incident response procedures contain stipulations concerning animals and plants accidentally or intentionally exposed to or infected with a select agent.

One commenter argued that the requirements in 7 CFR 331.14(a) and 9 CFR 121.14(a), which stipulate that regulated entities must develop and implement a written incident response plan based on a site-specific risk assessment, are misleading. The commenter stated that, since there is no standard methodology for conducting such risk assessments, the addition of specific issues that must be addressed by a risk assessment should be included in order to provide additional guidance for the regulated community. The commenter further observed that, in general, the risk assessment requirements for agricultural select agents and toxins are somewhat different from those for human select agents and toxins. The commenter concluded that a one size fits all approach may be overly burdensome or scientifically inaccurate.

We are making no changes based on this comment. The site-specific risk assessments required by the regulations in 7 CFR 331.14(a) and 9 CFR 121.14(a) are necessary in order to ensure the physical security of regulated entities. The risks cited by the commenter are matters of the biological risk presented by various select agents and toxins, which is a separate issue from the physical security of these select agents and toxins. The regulations are intended to prevent the theft, loss, or release of select agents and toxins. We also disagree with the commenter's assertion that there is no standard methodology for conducting site-specific risk assessments. We have developed guidance on this subject that may be found on the National Select Agent Registry at *www.selectagents.gov.*

We proposed to amend the regulations in 7 CFR 331.15 and 9 CFR 121.15, which concern provision of mandatory training for staff and visitors who work in or visit areas where select agents or toxins are handled or stored. We proposed to require all registered entities to provide security awareness and incident response training. We also proposed to establish that training for escorted personnel would be based on

the risk associated with accessing areas where select agents and toxins are used and/or stored. We further proposed to require that refresher training, currently required on an annual basis, also be provided if a registered entity's security, incident response, biosafety, or biocontainment plans are substantively altered. Finally, we proposed to specify that the responsible official ensure maintenance of training records. Currently there is no particular person designated as the entity's required recordkeeper, only that a training record must be kept.

One commenter suggested that 7 CFR 331.15(a) should specify that information and training on both biocontainment and biosafety be provided, as only information and training on biosafety had been specified in the proposed rule.

We agree with the commenter and have amended 7 CFR 331.15(a) in order to reflect the proper terminology in dealing with plant pathogens.

We proposed that the regulations in 7 CFR 331.15(a)(ii) concerning escorted personnel stipulate that training for such individuals must be based on the risk associated with accessing areas where select agents and toxins are used and/or stored. One commenter inquired what would represent an ''appropriate level of training.'' The commenter further wished to know how an entity would determine the risk associated with accessing such areas. Finally, the commenter asserted that there should be no need for non-approved individuals to potentially access areas where select agents and toxins are used and/or stored given that unsecured select agents or toxins could be moved elsewhere prior to the arrival of any escorted personnel.

We disagree with the commenter's assertion that non-approved individuals would never need to access areas where select agents and toxins are used and/or stored. For example, there may be a need for the repair of a refrigeration unit in a laboratory where employees are utilizing select agents or toxins as a part of concurrent research work. In addition, inventories of select agents and toxins may be large enough to make moving them impractical and overly time-consuming. It is therefore necessary for any visitors to know and understand the biological risks associated with the select agents or toxins used and/or stored in the area to which they will have access. This training would necessarily vary depending upon the areas that the escorted personnel would need to access, which would be determined by the entity. Visitors should ideally be made aware of the safety and security procedures as defined by the entity in question; however, we are leaving the regulations in their broadly written state in order to provide the greatest amount of flexibility for the wide variety of entities subject to the requirements.

We proposed to amend the regulations in 7 CFR 331.16 and 9 CFR 121.16, which concern the transfer of select agents and toxins from one registered entity to another, in order to codify practices for shipping, receiving, and storage of select agents and toxins to ensure that all registered entities have 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.

Two commenters asserted that the provisions concerning transfer are unclear with regard to the subject of the transfer of materials covered by the exemptions for diagnostic or clinical laboratories under 7 CFR 331.5, 9 CFR 121.5, and 9 CFR 121.6. The commenters requested that we clearly establish whether the new requirements supersede the existing provisions for transfer by exempt entities.

We are making no changes as a result of this comment. Those materials which qualify for exemption from the regulations have always been considered separately from the rest of the listed select agents or toxins. This may be a result of the exemptions granted for diagnostic or clinical laboratories, a result of a specific exemption request, or for other reasons which may be found in 7 CFR 331.5, 9 CFR 121.5, and 9 CFR 121.6. As a result, these materials are not subject to the regulations, including those portions of the regulations concerning transfers, apart from those sections pertaining to exemptions.

However, given that some commenters on the CDC proposed rule expressed confusion associated with the proposed provision, we have revised the language in order to clarify our original intent. Packaging of select agents and toxins for transfer must be made by an APHIS or CDC-approved individual.

The regulations in 7 CFR 331.17 and 9 CFR 121.17 concern required recordkeeping procedures for regulated entities as those records relate to select agents and toxins. We proposed to add language to address synthetic select agent organisms and animals and plants inoculated with select agents. We also proposed to add recordkeeping requirements whereby regulated entities maintain 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). As previously stated, we did not propose to require regulated entities to keep records regarding animals or plants exposed to select toxins.

Four commenters argued that counting individual vials of replicating biological agents is costly, burdensome, and a major source of frustration for investigators. The commenters went on to say that the requirement to measure volumes within each vial is problematic given both the ease with which volumes can change through natural processes and the difficulty in correctly assessing them in the frozen state during inventory verifications. The commenters stated that both counting vials and measuring volumes of individual vials are not effective means of increasing security.

We are making no changes to the regulations based on these comments. While we are aware of the burden resulting from the requirement to maintain an accurate and current inventory of each select agent and toxin held in long-term storage, we believe this is an essential element in establishing the security of select agents or toxins. We recognize that it may still be possible for an insider to steal a sample of an agent either from working stock or from an inventory without being detected; however, if an entity has a robust inventory management system, such incidents have a better chance of being detected. To assist registered entities in meeting the requirements for maintaining accurate inventories of materials in long term storage, we have developed guidance that may be found on the National Select Agent Registry at *www.selectagents.gov.* It should be noted that, while the volume measurements the commenter references are required for inventories of select toxins, they are not required in the case of inventory of select agents held in long-term storage due, in part, to the points raised by the commenter. However, we disagree with the commenter's assessment that measuring volume in the case of select toxins and counting vials in general as part of required inventory tracking of both select agents and toxins for registered entities is not necessary.

Another commenter stated that there is concern that the additional requirements for inventory each time a select agent is moved will adversely impact the viability and quality of the material in question.

We are making no changes as a result of this comment. In the case of those select agents and toxins in long-term

storage, collections of vials of materials can be recorded and grouped into tamper-evident containers and audits made of intact containers rather than audits of individual vials. This practice is stipulated in the current guidance document regarding long term storage, which is available on the National Select Agent Registry at *www.selectagents.gov.* Those select agents and toxins that are part of an entity's working stock are already in regular use and we therefore do not anticipate adverse effects arising from any required accounting.

Based on comments received on the CDC rule, we now recognize that there has been some confusion between those animals (including arthropods) and plants considered to be ''working stock'' and those considered to be ''inventory.'' To that end, we have developed guidance that will enable entities to better differentiate between these two categories. This guidance is available at *www.selectagents.gov.* It was not our intent to require a formal inventory of animals or plants intentionally or accidentally exposed to or infected with a select agent, but merely to state that entities should keep some record of such animals or plants. In order to clarify our intent regarding ''working stock'' and ''inventory,'' we are revising 7 CFR 331.17(a)(2) and 9 CFR 121.17(a)(2) to require an accurate, current accounting of any animals or plants intentionally or accidentally exposed to or infected with a select agent (including number and species, location, and appropriate disposition) instead of an accurate, current inventory of those animals or plants.

**Indirect and Economic Consequences**

Eight commenters requested that we consider the indirect consequences of continuing to include agents and toxins on the select agent list, the negative effect of the proposed rule changes on the potential workforce for select agent research, and the possibility that additional regulations concerning Tier 1 agents and toxins will mandate more Federal oversight and institutional compliance requirements, resulting in increased costs to taxpayers both directly and indirectly through reduced research efficiency. Commenters requested that the full economic and scientific impact of these added requirements be carefully assessed prior to implementation, especially the increased costs to academic institutions with no associated funding, and the increased burden on investigators already having difficulty finding time for research and experimentation. The commenters also stated that the timeline for implementation of the new requirements should be considered and disclosed to affected entities.

A cornerstone of the select agent program is to establish and enforce safety and security measures to prevent access to select agents and toxins for use in domestic or international terrorism or for any other criminal purpose. An equally important function of the select agent program is to ensure the appropriate availability of biological agents and toxins for research, education, and other legitimate purposes. To achieve both requires balancing the need for continuing biological research with requiring a level of safety and security commensurate with the risks posed by these select agents and toxins. We understand that safety and security requirements cost money and that money in the area of biological research is often a scarce commodity. We are, however, also aware that a lack of adequate safety and security requirements could result in damages measured not only in dollars but in human lives. It is our determination, based on the information available to us, that the additional requirements would, in many cases, codify systems and procedures already in use by a majority of regulated entities.

We are also renumbering several sections of the PPQ regulations so that they will match the numbering of the VS regulations, which we believe may be useful for those entities housing both PPQ select agents and toxins and VS select agents and toxins. As proposed, the section numbering did not match up because we did not propose to classify any PPQ select agents and toxins as Tier 1, so there were sections being added to the VS regulations that were not included in the PPQ regulations.

**Effective Date**

In response to comments received by the CDC requesting guidance and a timetable of when the proposed changes would need to be addressed, we have included a phase-in period for the effective date for certain requirements of the revised regulations, which should allow entities to comply without causing disruption or termination of research or educational projects. As noted in the ''Dates'' portion of this document, 60 days from the publication of the final rule, entities will be required to be in compliance with 7 CFR 331.1 through 331.10, 331.13, and 331.16 through 331.20 and 9 CFR 121.1 through 121.10, 121.13, 121.16, 121.17, and 121.20. One hundred and eighty days after the publication of the final rule, entities will be required to be in compliance with 7 CFR 331.11, 331.12, 331.14, and 331.15 and 9 CFR 121.11, 121.12, 121.13, 121.14, and 121.15.

The staggered effective dates for the provisions of the final rule are based on the effective dates previously used for a final rule published by the Select Agent Program on March 18, 2005 (70 FR 13242–13292, Docket No. 02–088–4). If the regulated community has concerns about the established timeline, they can contact the Federal select agent program for technical assistance.

Therefore, for the reasons given in the proposed rule and in this document, we are adopting the proposed rule as a final rule, with the changes discussed in this document.

**Executive Orders 12866 and 13563 and Regulatory Flexibility Act**

This final rule has been determined to be significant/economically significant for the purposes of Executive Order 12866 and, therefore, has been reviewed by the Office of Management and Budget.

We have prepared an economic analysis for this rule. The economic analysis provides a cost-benefit analysis, as required by Executive Orders 12866 and 13563, which 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, and equity). Executive Order 13563 emphasizes the importance of quantifying both costs and benefits, of reducing costs, of harmonizing rules, and of promoting flexibility. The economic analysis also provides a final regulatory flexibility analysis that examines the potential economic effects of this rule on small entities, as required by the Regulatory Flexibility Act. The economic analysis is summarized below. Copies of the full analysis are available on the Regulations.gov Web site (see footnote 1 in this document for a link to Regulations.gov) or by contacting the person listed under **FOR FURTHER INFORMATION CONTACT**.

Based on information obtained through site-specific inspections, we believe most registered entities already have in place many of the information security requirements set forth in the final rule, and compliance costs of the rules are therefore expected to be minimal. Entities more likely to be affected will be laboratories and other institutions conducting research and related activities that involve the use of select agents and toxins categorized as Tier 1. These entities will be required to conduct a pre-access suitability

assessment of individuals with access to a Tier 1 select agent or toxin, as well as enroll these individuals in an occupational health program.

The rule would reduce the period that FBI background checks are valid from five to three years. This increased frequency would effectively increase the cost of background checks by 67 percent. Based on the current number of individuals required to have the background checks, we estimate that the present value of these government-borne costs over five years will increase by $1.96 million across all registered entities. The annual increase in costs will total about $432,000.

While we expect few if any of the registered entities to incur significant compliance costs, required documentation of measures already regularly performed with respect to biocontainment/biosafety, incident response, information security, and ongoing suitability assessment may require additional time of personnel. We estimate additional recurring costs related to information security, such as for software updates, could total about $2 million per year, or about $5,500 per entity, in the unlikely event that none of the entities already uses equivalent information security measures. As noted, many of these costs are already currently borne by entities in their conduct of generally recognized best practices.

For entities possessing a Tier 1 agent or toxin, the costs of pre-access suitability assessments and occupational health programs are estimated to total between $2.8 million and $4.4 million, or between about $9,600 and $15,100 per entity, on average. Again, actual costs incurred are unlikely to reach these maximum cost ranges; we expect that many of the entities with a Tier 1 agent or toxin already conduct assessments and have health programs similar or equivalent to those required by the final rules.

The benefits of strengthened safeguards against the unintentional or deliberate release of a select agent or toxin greatly exceed compliance costs of the rules. As an example of losses that can occur, the October 2001 anthrax attacks caused 5 fatalities and 17 illnesses, disrupted business and government activities (including $2 billion in lost revenues for the Postal Service), and required more than $23 million to decontaminate one Senate office building and $3 billion to decontaminate postal facilities and procure mail-sanitizing equipment. Deliberate introduction greatly increases the probability of a select agent becoming established and causing wide-ranging and devastating impacts to the economy, other disruptions to society, and diminished confidence in public and private institutions.

The amended regulations will enhance the protection of human, animal, and plant health and safety. The final rules will reduce likelihood of the accidental or intentional release of a select agent or toxin. Benefits of the rules will derive from the greater probability that a release will be prevented from occurring. While the total cost of implementing the regulations is estimated to range between $2.8 million–$4.4 million across all entities with a Tier 1 agent or toxin and approximately $2.4 million in annual cost across all registered entities and the Federal Government, we believe many of these costs are currently incurred by affected entities as generally recognized practices.

**Executive Order 12372**

This program/activity is listed in the Catalog of Federal Domestic Assistance under No. 10.025 and is subject to Executive Order 12372, which requires intergovernmental consultation with State and local officials. (See 7 CFR part 3015, subpart V.)

**Executive Order 12988**

This final rule has been reviewed under Executive Order 12988, Civil Justice Reform. This rule: (1) Preempts all State and local laws and regulations that are inconsistent with this rule; (2) has no retroactive effect; and (3) does not require administrative proceedings before parties may file suit in court challenging this rule.

**Executive Order 13175**

This rule has been reviewed in accordance with the requirements of Executive Order 13175, Consultation and Coordination with Indian Tribal Governments. The review reveals that this regulation will not have substantial and direct effects on Tribal governments and will not have significant Tribal implications.

**Paperwork Reduction Act**

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 final rule have been submitted for approval to the Office of Management and Budget (OMB). When OMB notifies us of its decision, we will publish a document in the **Federal Register** providing notice of the assigned OMB control numbers or, if approval is denied, providing notice of what action we plan to take.

**E-Government Act Compliance**

The Animal and Plant Health Inspection Service is committed to compliance with the E-Government Act to promote the use of the Internet and other information technologies, to provide increased opportunities for citizen access to Government information and services, and for other purposes. For information pertinent to E-Government Act compliance related to this rule, please contact Mrs. Celeste Sickles, APHIS' Information Collection Coordinator, at (301) 851–2908.

**List of Subjects**

*7 CFR Part 331*

Agricultural research, Laboratories, Plant diseases and pests, Reporting and recordkeeping requirements.

*9 CFR Part 121*

Agricultural research, Animal diseases, Laboratories, Medical research, Reporting and recordkeeping requirements.

Accordingly, we are amending 7 CFR part 331 and 9 CFR part 121 as follows:

**Title 7**

## PART 331—POSSESSION, USE, AND TRANSFER OF SELECT AGENTS AND TOXINS

■ 1. The authority citation for part 331 continues to read as follows:

**Authority:** 7 U.S.C. 8401; 7 CFR 2.22, 2.80, and 371.3.

■ 2. Section 331.1 is amended as follows:

■ a. In the introductory text of the definition of *biological agent,* by removing the word ''rickettsiae,'';

■ b. By adding, in alphabetical order, definitions of *information security, recombinant nucleic acids, security barrier,* and *synthetic nucleic acids; and*

■ c. In the introductory text of the definition of *toxin,* by removing the word ''rickettsiae,''.

The additions read as follows:

**§ 331.1 Definitions.**

* * * * *

*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 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.

* * * * *

*Recombinant nucleic acids.* (1) Molecules that are constructed by joining nucleic acid molecules and that can replicate in a living cell (i.e., recombinant nucleic acids); or

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

* * * * *

*Security barrier.* A physical structure that is designed to prevent entry by unauthorized persons, animals, or materials.

* * * * *

*Synthetic nucleic acids.* (1) Molecules that are chemically or by other means synthesized or amplified, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules (i.e., synthetic nucleic acids); or

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

* * * * *

■ 3. Section 331.3 is amended as follows:

■ a. By revising paragraph (b);

■ b. In paragraph (c) introductory text, by adding the words ''and/or synthetic'' after the word ''recombinant'' each time it appears.

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

■ d. By adding paragraph (d)(3); and

■ e. By revising paragraph (e)

The revisions and addition read as follows:.

**§ 331.3 PPQ select agents and toxins.**

* * * * *

(b) PPQ select agents and toxins: *Peronosclerospora philippinensis* (*Peronosclerospora sacchari*); *Phoma glycinicola* (formerly *Pyrenochaeta glycines*); *Ralstonia solanacearum*; *Rathayibacter toxicus*; *Sclerophthora rayssiae*; *Synchytrium endobioticum*; *Xanthomonas oryzae.*

* * * * *

(d) * * *

(3) Any subspecies of *Ralstonia solanacearum* except race 3, biovar 2 and all subspecies of *Sclerophthora rayssiae* except var. *zeae,* provided that the individual or entity can verify that the agent is within the exclusion category.

(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 Administrator that the attenuated strain or inactivated toxin does not pose a severe threat to plant health or plant 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.

* * * * *

■ 4. Section 331.9 is amended as follows:

■ a. In paragraph (a)(4), by removing the word ''and'';

■ b. By redesignating paragraph (a)(5) as paragraph (a)(6);

■ c. By adding a new paragraph (a)(5);

■ d. By revising the first sentence of paragraph (b)

The addition and revision read as follows:.

**§ 331.9 Responsible official.**

(a) * * *

(5) Have a physical (and not merely a telephonic or audio/visual) presence at the registered entity to ensure that the entity is in compliance with the select agent regulations and be able to respond in a timely manner to onsite incidents involving select agents and toxins in accordance with the entity's incident response plan; 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.

* * *

* * * * *

■ 5. Section 331.10 is amended as follows:

■ a. By redesignating paragraphs (e) through (i) as paragraphs (f) through (j) respectively;

■ b. By adding a new paragraph (e); and

■ c. In newly redesignated paragraph (i), by removing the number ''5'' and adding the number ''3'' in its place.

The addition reads as follows:

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

* * * * *

(e) A person with valid approval from the HHS Secretary or Administrator to have access to select agents or toxins may request, through his or her Responsible Official, that the HHS Secretary or Administrator provide their approved access status to another registered individual or entity for a specified period of time.

* * * * *

■ 6. Section 331.11 is amended as follows:

■ a. By revising paragraph (b);

■ b. By revising paragraph (c)(2);

■ c. In paragraph (c)(6), by removing the word ''and'';

■ d. In paragraph (c)(7), by removing the period and adding a semicolon in its place;

■ e. By adding new paragraphs (c)(8), (9), and (10);

■ f. By redesignating paragraphs (e) and (f) as paragraphs (g) and (h), respectively;

■ g. By adding new paragraphs (e) and reserved (f); and

■ h. By revising newly redesignated paragraph (g).

The revisions and additions read as follows:

**§ 331.11 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 (including arthropods) 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 describe procedures for how the entity will notify the appropriate Federal, State, or local law enforcement agencies of such activity.

(9) Contain provisions for information security that:

(i) Ensure that all external connections to systems which manage security for the registered space are isolated or have controls that permit only authorized and authenticated users;

(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 agents and toxins 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 viruses, worms, spyware) from compromising the confidentiality, integrity, or availability of information systems which manage access to spaces registered under this part or records as specified in § 331.17;

(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, surveillance devices, and/or systems that manage the requirements of § 331.17 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) Entities must conduct complete inventory audits of all affected select agents and toxins in long-term storage when any of the following occur:

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

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

(3) In the event of a theft or loss of a select agent or toxin, all select agents and toxins under the control of that principal investigator.

(f) [Reserved]

(g) In developing a security plan, an individual or entity should consider the documents entitled, ''Security Guidance for Select Agent or Toxin Facilities.'' This document is available on the National Select Agent Registry at *http://www.selectagents.gov/*.

■ 7. Section 331.12 is amended as follows:

■ a. By revising paragraph (a);

■ b. By redesignating paragraph (d) as paragraph (e); and

■ c. By adding reserved paragraph (d).

The revision reads as follows:

**§ 331.12 Biocontainment.**

(a) An individual or entity required to register under this part must develop and implement a written biocontainment plan that is commensurate with the risk of the select agent or toxin, given its intended use.[4] The biocontainment plan must contain sufficient information and documentation to describe the containment procedures for the select agent or toxin, including any animals or plants intentionally or accidentally exposed to or infected with a select agent.

* * * * *

■ 8. Section 331.13 is amended by removing footnote 5 and revising paragraph (a) to read as follows:

**§ 331.13 Restricted experiments.**

(a) An individual or entity may not conduct, or possess products resulting from, the following experiments unless approved by and conducted in accordance with the conditions prescribed by the Administrator:

(1) Experiments that involve the deliberate transfer of, or selection for, a drug or chemical resistance trait to select agents that are not known to acquire the trait naturally, if such acquisition could compromise the control of disease agents in humans, veterinary medicine, or agriculture.

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

* * * * *

■ 9. Section 331.14 is amended as follows:

■ a. In the section heading, by redesignating footnote 6 as footnote 5;

■ b. By revising the first sentence in paragraph (a);

■ c. By redesignating footnote 7 as footnote 6;

■ d. By revising paragraph (b);

■ e. By redesignating paragraphs (c) and (d) as paragraphs (d) and (f), respectively; and

■ f. By adding new paragraphs (c) and reserved (e).

The revisions and additions read as follows:

**§ 331.14 Incident response.[5]**

(a) An individual or entity required to register under this part must develop and implement a written incident response plan[6] based upon a site specific risk assessment. * * *

(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, and other natural and man-made events.

(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 (including arthropods) or plants intentionally or accidentally exposed to or infected with a select agent.

* * * * *

■ 10. Section 331.15 is revised to read as follows:

**§ 331.15 Training.**

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

(1) 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; and

(2) 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) [Reserved]

(c) Refresher training must be provided annually for individuals with access approval from the HHS Secretary or Administrator or at such time as the

[4] Technical assistance and guidance may be obtained by contacting APHIS.

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

[6] Technical assistance and guidance may be obtained by contacting APHIS.

registered individual or entity significantly amends its security, incident response, or biocontainment plans.

(d) The responsible official must ensure a record of the training provided to each individual with access to select agents and toxins 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.

■ 11. Section 331.16 is amended as follows:

■ a. By redesignating footnote 8 as footnote 7;

■ b. By redesignating paragraphs (e) through (h) as paragraphs (h), (i), (j), and (f) respectively;

■ c. By adding a new paragraph (e);

■ d. In newly redesignated paragraph (f), by removing the words ''packaging and''; and

■ e. By adding a new paragraph (g).

The additions read as follows:

**§ 331.16 Transfers.**

* * * * *

(e) After authorization is provided by APHIS or CDC, the packaging of the select agent(s) and toxin(s) is performed by an individual approved by the HHS Secretary or Administrator to have access to select agents and toxins and is in compliance with all applicable laws concerning packaging.

* * * * *

(g) 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.

* * * * *

■ 12. Section 331.17 is amended as follows:

■ a. By revising paragraph (a)(1) introductory text;

■ b. By redesignating paragraphs (a)(2) through (6) as paragraphs (a)(3) through (7), respectively; and

■ c. By adding a new paragraph (a)(2).

The revision and addition read as follows:

**§ 331.17 Records.**

(a) * * *

(1) An accurate, current inventory for each select agent (including viral genetic elements, recombinant and/or synthetic nucleic acids, and organisms containing recombinant and/or synthetic nucleic acids) 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 accounting of any animals or plants intentionally or accidentally exposed to or infected with a select agent (including number and species, location, and appropriate disposition);

* * * * *

**§ 331.19 [Amended]**

■ 13. Section 331.19 is amended as follows:

■ a. By removing paragraph (b)(1)(iv); and

■ b. By redesignating paragraphs (b)(1)(v) through (b)(1)(viii) as paragraphs (b)(1)(iv) through (b)(1)(vii), respectively.

■ 14. Section 331.20 is revised to read as follows:

**§ 331.20 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 Administrator 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 Administrator within 180 calendar days of the decision.

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

**Title 9**

## PART 121—POSSESSION, USE, AND TRANSFER OF SELECT AGENTS AND TOXINS

■ 15. The authority citation for part 121 continues to read as follows:

**Authority:** 7 U.S.C. 8401; 7 CFR 2.22, 2.80, and 371.4.

■ 16. Section 121.1 is amended as follows:

■ a. In the introductory text of the definition of *biological agent,* by removing the word ''rickettsiae,'';

■ b. By adding, in alphabetical order, definitions of *information security, occupational exposure, recombinant nucleic acids, security barrier,* and *synthetic nucleic acids;* and

■ c. In the introductory text of the definition of *toxin,* by removing the word ''rickettsiae,''.

The additions read as follows:

**§ 121.1 Definitions.**

* * * * *

*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 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.

* * * * *

*Occupational exposure.* Any reasonably anticipated skin, eye, mucous membrane, parenteral contact, or respiratory aerosol exposure to select agents or toxins that may result from the performance of an employee's duties.

* * * * *

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

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

* * * * *

*Security barrier.* A physical structure that is designed to prevent entry by unauthorized persons.

* * * * *

*Synthetic nucleic acids.* (1) Molecules that are chemically or by other means synthesized or amplified, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules (i.e., synthetic nucleic acids); or

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

* * * * *

■ 17. Section 121.3 is amended as follows:

■ a. By adding a sentence at the end of paragraph (a);

■ b. By revising paragraph (b);

■ c. In paragraph (c) introductory text, by adding the words ''and/or synthetic'' after the word ''recombinant'' each time it appears;

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

■ e. By adding paragraph (d)(3);

■ f. By revising paragraph (e); and

■ g. In paragraph (f)(3)(i), by removing the words ''Newcastle disease virus''(velogenic)'' and adding the words ''virulent Newcastle disease virus'' in their place.

The revisions and additions read as follows:

**§ 121.3 VS 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) VS select agents and toxins: African horse sickness virus; African swine fever virus; Avian influenza virus; Classical swine fever virus; *Foot-and-mouth disease virus; Goat pox virus; Lumpy skin disease virus; *Mycoplasma capricolum*; *Mycoplasma mycoides*; Newcastle disease virus; [1] Peste des petits ruminants virus; *Rinderpest virus; Sheep pox virus; Swine vesicular disease virus.

* * * * *

(d) * * *

(3) Any low pathogenic strains of avian influenza virus, any strain of Newcastle disease virus which does not meet the criteria for virulent Newcastle disease virus, all subspecies *Mycoplasma capricolum* except subspecies *capripneumoniae* (contagious caprine pleuropneumonia), and all subspecies *Mycoplasma mycoides* except subspecies *mycoides* small colony (*Mmm* SC) (contagious bovine pleuropneumonia), provided that the individual or entity can verify that the agent is within the exclusion category.

(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 Administrator that the attenuated strain or inactivated toxin does not pose a severe threat 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/*.

[1] A virulent Newcastle disease virus (avian paramyxovirus serotype 1) has an intracerebral pathogenicity index in day-old chicks (*Gallus gallus*) of 0.7 or greater or has an amino acid sequence at the fusion (F) protein cleavage site that is consistent with virulent strains of Newcastle disease virus. A failure to detect a cleavage site that is consistent with virulent strains does not confirm the absence of a virulent virus.

(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.

* * * * *

■ 18. Section 121.4 is amended as follows:

■ a. By adding a sentence at the end of paragraph (a);

■ b. By revising paragraph (b);

■ c. In paragraph (c) introductory text, by adding the words ''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 adding paragraph (d)(3);

■ f. By revising paragraph (e); and

■ g. 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.

The revisions and additions read as follows:

**§ 121.4 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; Bacillus anthracis* (Pasteur strain); *Brucella abortus; Brucella melitensis; Brucella suis; *Burkholderia mallei; *Burkholderia pseudomallei;* Hendra virus; Nipah virus; Rift Valley fever virus; Venezuelan equine encephalitis virus.

* * * * *

(d) * * *

(3) Any subtypes of Venezuelan equine encephalitis virus except for Subtypes IAB or IC, provided that the individual or entity can verify that the agent is within the exclusion category.

(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.

* * * * *

**§ 121.5 [Amended]**

■ 19. In § 121.5, paragraph (a)(3)(i) is amended by removing the words ''bovine spongiform encephalopathy agent,''.

■ 20. Section 121.6 is amended as follows:

■ a. In paragraph (a)(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; and

■ b. By revising paragraph (e) to read as follows:

**§ 121.6 Exemptions for overlap select agents and toxins.**

* * * * *

(e) The Administrator may exempt an individual or entity from the requirements of this part for 30 calendar days if it is necessary to respond to a domestic or foreign agricultural emergency involving an overlap select agent or toxin. The Administrator may extend the exemption once for an additional 30 days.

* * * * *

■ 21. Section 121.9 is amended as follows:

■ a. In paragraph (a)(4), by removing the word ''and'';

■ b. By redesignating paragraph (a)(5) as paragraph (a)(6);

■ c. By adding a new paragraph (a)(5);

■ d. By revising the first sentence of paragraph (b); and

■ e. By revising the first sentence of paragraph (c)(1).

The addition and revisions read as follows:

**§ 121.9 Responsible official.**

(a) * * *

(5) Have a physical (and not merely a telephonic or audio/visual) presence at the registered entity to ensure that the entity is in compliance with the select agent regulations and be able to respond in a timely manner to onsite incidents involving select agents and toxins in

accordance with the entity's incident response plan; 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.

* * *

(c) * * *

(1) The identification of any of the following select agents or toxins must be immediately reported by telephone, facsimile, or email: African horse sickness virus, African swine fever virus, avian influenza virus (highly pathogenic), *Bacillus anthracis, Burkholderia mallei, Burkholderia pseudomallei,* classical swine fever virus, foot-and-mouth disease virus, virulent Newcastle disease virus, rinderpest virus, and swine vesicular disease virus. * * *

* * * * *

■ 22. Section 121.10 is amended as follows:

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

■ b. By adding a new paragraph (e); and

■ c. In newly redesignated paragraph (j), by removing the number ''5'' and adding the number ''3'' in its place.

The addition reads as follows:

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

* * * * *

(e) A person with valid approval from the HHS Secretary or Administrator to have access to select agents or toxins may request, through his or her Responsible Official, that the HHS Secretary or Administrator provide their approved access status to another registered individual or entity for a specified period of time.

* * * * *

■ 23. Section 121.11 is amended as follows:

■ a. By revising paragraph (b);

■ b. By revising paragraph (c)(2);

■ c. In paragraph (c)(6), by removing the word ''and'';

■ d. By adding new paragraphs (c)(8), (9), and (10);

■ e. By redesignating paragraphs (e) and (f) as paragraphs (g) and (h), respectively;

■ f. By adding new paragraphs (e) and (f); and

■ g. By revising newly redesignated paragraph (g).

The revisions and additions read as follows:

**§ 121.11 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 describe procedures for how the entity will notify the appropriate Federal, State, or local law enforcement agencies of such activity.

(9) Contain provisions for information security that:

(i) Ensure that all external connections to systems which manage security for the registered space are isolated or have controls that permit only authorized and authenticated users;

(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 agents and toxins 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 viruses, worms, spyware) from compromising the confidentiality, integrity, or availability of information systems which manage access to spaces registered under this part or records as specified in § 121.17;

(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, surveillance devices, and/or systems that manage the requirements of § 121.17 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) Entities must conduct complete inventory audits of all affected select agents and toxins in long-term storage when any of the following occur:

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

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

(3) In the event of a theft or loss of a select agent or toxin, all select agents and toxins under the control of that principal investigator.

(f) 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 employees with access to Tier 1 select agents and toxins on entity policies and procedures for reporting, evaluation, and corrective actions concerning the assessment of personnel suitability; 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 the following security enhancements:

(i) Procedures that will limit access to a Tier 1 select agent or toxin to only those individuals who are approved by the HHS Secretary or Administrator

following a security risk assessment by the Attorney General, have had an entity-conducted pre-access suitability assessment, and are subject to the entity's procedures for ongoing suitability assessment;

(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 that are based on the entity's site-specific risk assessment;

(iv) A minimum of three security barriers where each security barrier adds to the delay in reaching secured areas where select agents and toxins are used or stored. One of the security barriers must be monitored in such a way as to detect intentional and unintentional circumventing of established access control measures under all conditions (day/night, severe weather, etc.) The final barrier must limit access to the select agent or toxin to personnel approved by the HHS Secretary or Administrator, following a security risk assessment by the Attorney General.

(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) For powered access control systems, describe procedures to ensure that security is maintained in the event of the failure of access control systems due to power disruption affecting registered space;

(viii) The entity must:

(A) Determine that the response time for security forces or local police will not exceed 15 minutes where the response time is measured from the time of an intrusion alarm, or report of a security incident, to the arrival of the responders at the first security barrier or;

(B) Provide security barriers that are sufficient to delay unauthorized access until the response force arrives in order to safeguard the select agents and toxins from theft, intentional release, or unauthorized access. The response time is measured from the time of an intrusion alarm, or report of a security incident, to the arrival of the responders at the first security barrier.

(5) Entities that possess foot-and-mouth disease virus and rinderpest virus must have the following additional security requirements:

(i) A minimum of four barriers, one of which must be a perimeter security fence or equivalent which is monitored 24 hours a day, 7 days a week (24/7) to detect the presence of unauthorized persons, vehicles, materials, or unauthorized activities;

(ii) Onsite 24/7 armed security response force with roving patrol. Response time must not exceed 5 minutes from the time of an intrusion alarm or report of a security incident;

(iii) CCTV surveillance with 24/7 monitoring and recording; and

(iv) Transport vehicle with GPS tracking designed to serve as a containment vehicle.

(g) In developing a security plan, an individual or entity should consider the document entitled, ''Security Guidance for Select Agent or Toxin Facilities.'' This document is available on the Internet at *http://www.selectagents.gov/*.

* * * * *

■ 24. Section 121.12 is amended as follows:

■ a. By revising paragraph (a);

■ b. By revising paragraph (c)(1);

■ c. By adding a second sentence to paragraph (c)(2);

■ d. In paragraph (c)(3), by removing the address ''*http://www.aphis.usda.gov/programs/ag_selectagent/index.html*'' and adding in its place ''*http://www.selectagents.gov/*'';

■ e. By redesignating paragraph (d) as paragraph (e); and

■ f. By adding a new paragraph (d).

The revisions and addition read as follows:

**§ 121.12 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.[9] 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 (including arthropods) 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 National Select Agent Registry at *http://www.selectagents.gov/*.

(2) * * * This document is available on the National Select Agent Registry 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.

* * * * *

■ 25. Section 121.13 is amended by removing footnote 10 and revising paragraphs (a) and (b) to read as follows:

**§ 121.13 Restricted experiments.**

(a) An individual or entity may not conduct, or possess products (i.e., select agents that are not known to acquire a drug resistance trait naturally, if such acquisition could compromise the control of disease agents in humans, veterinary medicine, or agriculture, or recombinant and/or synthetic nucleic acids containing genes for the biosynthesis of select toxins lethal for vertebrates at an LD[50] < 100 ng/kg body weight) resulting from, the following experiments unless approved by and conducted in accordance with the conditions prescribed by the Administrator:

(b) *Restricted experiments:* (1) Experiments that involve the deliberate transfer of, or selection for, a drug resistance trait to select agents that are not known to acquire the trait naturally, if such acquisition could compromise the control of disease agents in humans, veterinary medicine, or agriculture.

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

* * * * *

■ 26. Section 121.14 is amended as follows:

■ a. In the section heading, by redesignating footnote 11 as footnote 10;

■ b. In paragraph (a), by redesignating footnote 12 as footnote 11 and revising the first sentence of paragraph (a);

■ c. By revising paragraph (b);

■ d. By redesignating paragraphs (c) and (d) as paragraphs (d) and (f), respectively; and

■ e. By adding new paragraphs (c) and (e).

The revisions and additions read as follows:

[9] Technical assistance and guidance may be obtained by contacting APHIS.

**§ 121.14 Incident response.[10]**

(a) An individual or entity required to register under this part must develop and implement a written incident response plan [11] based upon a site specific risk assessment. * * *

(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, and other natural and man-made events.

(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 (including arthropods) 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 procedures for how the entity will notify the appropriate Federal, State, or local law enforcement agencies of suspicious activity that may be criminal in nature and related to the entity, its personnel, or its select agents or toxins.

* * * * *

■ 27. Section 121.15 is revised to read as follows:

**§ 121.15 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 to:

(1) 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; and

(2) 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 for individuals with access approval from the HHS Secretary or Administrator 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 toxins 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.

■ 28. Section 121.16 is amended as follows:

■ a. By redesignating footnote 14 as footnote 12;

■ b. By redesignating paragraphs (f) through (i) as paragraphs (i), (j), (k), and (g), respectively;

■ c. By adding a new paragraph (f);

■ d. In newly redesignated paragraph (g), by removing the words ''packaging and''; and

■ e. By adding a new paragraph (h).

The additions read as follows:

**§ 121.16 Transfers.**

* * * * *

(f) After authorization is provided by APHIS or CDC, the packaging of the select agent(s) and toxin(s) is performed by an individual approved by the HHS Secretary or Administrator to have access to select agents and toxins and is in compliance with all applicable laws concerning packaging.

* * * * *

(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.

* * * * *

■ 29. Section 121.17 is amended as follows:

■ a. By revising paragraph (a)(1) introductory text;

■ b. By redesignating paragraphs (a)(2) through (6) as paragraphs (a)(3) through (7), respectively; and

■ c. By adding a new paragraph (a)(2).

The revision and addition read as follows:

**§ 121.17 Records.**

(a) * * *

(1) An accurate, current inventory for each select agent (including viral genetic elements, recombinant and/or synthetic nucleic acids, and organisms containing recombinant and/or synthetic nucleic acids) 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 accounting of any animals or plants intentionally or accidentally exposed to or infected with a select agent (including number and species, location, and appropriate disposition);

* * * * *

■ 30. Section 121.20 is revised to read as follows:

**§ 121.20 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 Administrator 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 Administrator within 180 calendar days of the decision.

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

Done in Washington, DC, this 28th day of September 2012.

**Edward Avalos,**

*Under Secretary for Marketing and Regulatory Programs.*

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BILLING CODE 3410–34–P

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

[11] Technical assistance and guidance may be obtained by contacting APHIS.