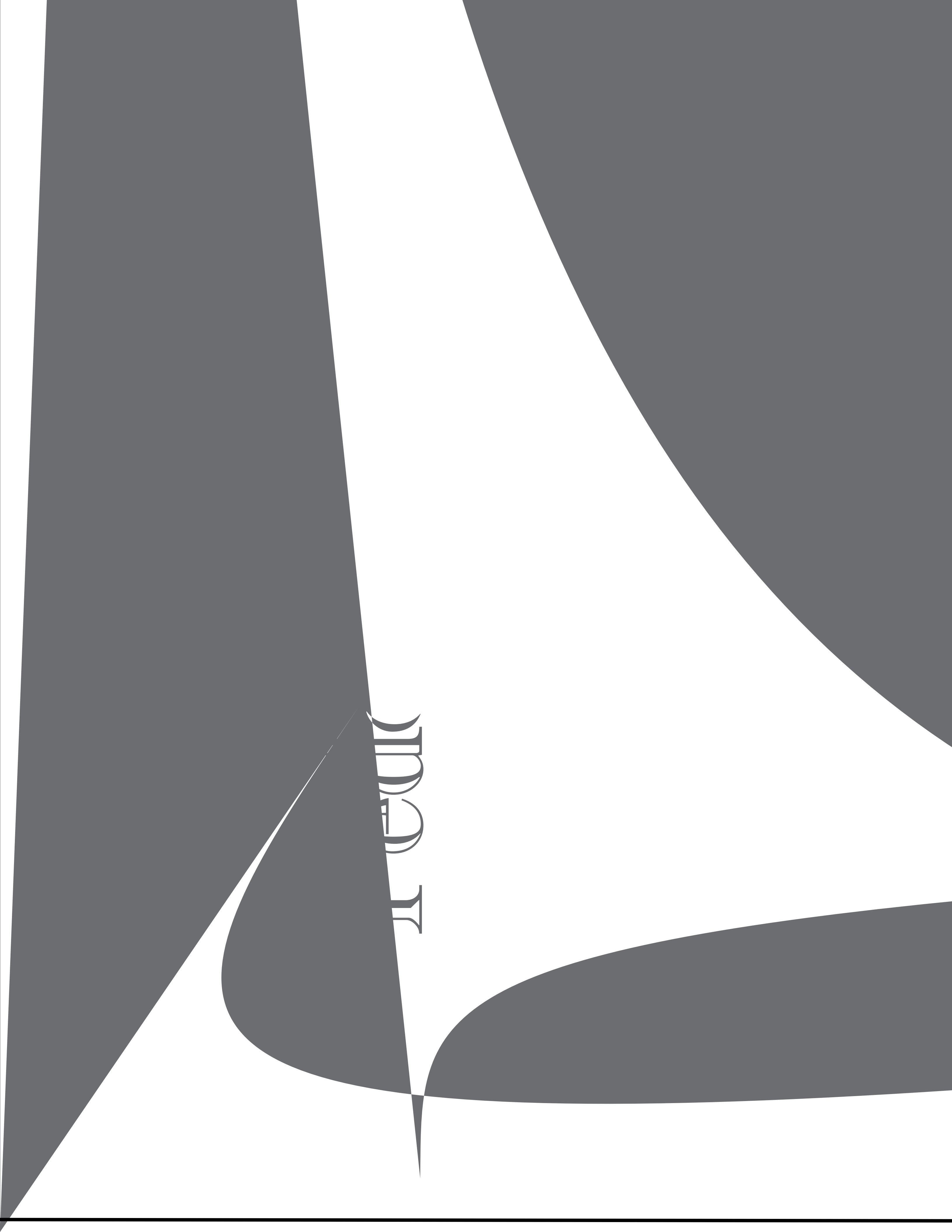

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Animal and Plant Health Inspection Service, USDA.

Final rule.

We are adopting as a final rule, with changes, an interim rule that established regulations governing the possession, use, and transfer of biological agents and toxins that have been determined to have the potential to pose a severe threat to public health and

interim rules for 60 days ending January 2, 2004. We did not receive any comments by that date.

APHIS and CDC collaborated closely on the December 13, 2002, and November 3, 2003, interim rules, as well as on this final rule and CDC's final rule also issued in today's . Below is a summary of the changes we are making to the regulations in this final rule. We refer to the regulations in place prior to the effective date of this final rule as the ''interim'' regulations, or ''interim'' 7 CFR 331.4, for example, when we need to distinguish between

contained in a specimen presented for proficiency testing.

19. We are amending the provisions relating to access approvals to state that an individual will be deemed to have access at any point in time if the individual has possession of a select agent or toxin (*e.g.*, carries, uses, or manipulates) or the ability to gain possession of a select agent or toxin.

20. We are amending the provisions pertaining to access approval to provide that an individual's access approval may be revoked if the individual is within any of the categories specified in the regulations.

21. We are amending the security sections to clarify that the security plan must be sufficient to safeguard the select agent or toxin against unauthorized access, theft, loss, or release.

22. We are adding the provisions for restricted experiments to 7 CFR part 331 and we are amending these provisions in 7 CFR part 331 and 9 CFR part 121 to indicate that these experiments must be conducted under any conditions prescribed by the Administrator.

23. We are amending the training sections to require that information and training on biocontainment/biosafety and security be provided to each individual with access approval from the Administrator or the HHS Secretary before he/she has access and to each individual not approved for access by the Administrator or the HHS Secretary before he/she works in or visits areas where select agents or toxins are handled or stored (*e.g.*, laboratories, growth chambers, animal rooms, greenhouses, storage areas, etc.).

24. We are amending the transfer section in 9 CFR 121.16 to set out the requirements for transfer of a select agent or toxin contained in a specimen for proficiency testing.

25. We are amending the transfer sections to provide that, on a case-by-case basis, the Administrator may authorize a transfer of a select agent or toxin not otherwise eligible for transfer under the regulations under conditions prescribed by the Administrator.

26. We are amending the transfer sections to provide that an authorization for a transfer shall be valid only for 30 calendar days after issuance, except that such an authorization becomes immediately null and void if any facts supporting the authorization changes (*e.g.*, change in the certificate of registration for the sender or recipient, change in the application for transfer).

27. We are amending the records sections to require the maintenance of an accurate, current inventory for each toxin held and for each select agent held in long-term storage (placement in a system designed to ensure viability for future use, such as in a freezer or lyophilized materials).

28. We are amending the section pertaining to notification of theft, loss, or release in 7 CFR part 331 to require that APHIS or CDC be notified immediately upon discovery of a release of a select agent or toxin outside of the primary barriers of the biocontainment area and we are amending this section in 9 CFR part 121 to require that APHIS or CDC be notified immediately upon discovery of a release of a select agent or toxin causing occupational exposure or a release outside of the primary barriers of the biocontainment area.

29. We are amending the administrative review sections to allow an individual to appeal revocation of access approval.

APHIS and CDC are revising the format of the regulations in the final rules so that the section numbers and, to the extent possible, the section titles and the information contained in each section is the same in 7 CFR part 331, 9 CFR part 121, and 42 CFR part 73. These changes should make the regulations easier to use and facilitate compliance. The chart below sets out the format of 7 CFR part 331 and 9 CFR part 121 set by the interim rules (interim regulations) and the new format for the regulations in 7 CFR part 331 and 9 CFR part 121 (final rule).

1.0 *Effective and applicability dates*	
121.0 *Effective and applicability dates*	
1.1 *Definitions*	1.1 *Definitions.*
121.1 *Definitions*	121.1 *Definitions.*
1.2 *Purpose and scope*	1.2 *Purpose and scope.*
121.2 *Purpose and scope*	121.2 *Purpose and scope.*
1. *List of biological agents and toxins*	1. *PPQ select agents and toxins.*
121. *List of biological agents and toxins*	121. *VS select agents and toxins.*
1. *Exemptions*	1. *[Reserved].*
121. *Exemptions for overlap agents or toxins*	121. *Overlap select agents and toxins.*
1. *Registration; who must register*	1. *Exemptions.*
121. *Exemptions for animal agents and toxins*	121. *Exemptions for VS select agents and toxins.*
1. *Registration; general provisions*	1. *[Reserved]*
121. *Registration; who must register*	121. *Exemptions for overlap select agents and toxins.*
1. *Denial, revocation, or suspension of registration*	1. *Registration and related security risk assessments.*
121. *Registration; general provisions*	121. *Registration and related security risk assessments.*
1. *Registration; how to register*	1. *Denial, revocation, or suspension of registration.*
121. *Denial, revocation, or suspension of registration*	121. *Denial, revocation, or suspension of registration.*
1[illegible] *Responsibilities of the responsible official*	1[illegible] *Responsible official.*
121[illegible] *Registration; how to register*	121[illegible] *Responsible official.*
1.10 *Restricting access to biological agents and toxins*	1.10 *Restricting access to select agents and toxins; security risk assessments.*
121.10 *Responsibilities of the responsible official*	121.10 *Restricting access to select agents and toxins; security risk assessments.*
1.11 *Biocontainment and security plan*	1.11 *Security.*
121.11 *Restricting access to biological agents and toxins*	121.11 *Security.*
1.12 *Training*	1.12 *Biocontainment.*
121.12 *Biosafety and security plan*	121.12 *Biosafety.*
1.1 *Transfer of biological agents and toxins*	1.1 *Restricted experiments.*
121.1 *Training*	121.1 *Restricted experiments.*
1.1 *Records*	1.1 *Incident response.*

121.1 *Records*	121.1 *Training.*
1.1 *Notification in the event of theft, loss, or release of a biological agent or toxin*.	1.1 *Transfers.*
121.1 *Inspections*	121.1 *Transfers.*
1.1 *Administrative review*	1.1 *Records.*
121.1 *Notification in the event of theft, loss, or release of a biological agent or toxin*.	121.1 *Records.*
121.1 *Administrative review*	1.1 *Inspections.*
	121.1 *Inspections.*
	1.[illegible] *Notification of theft, loss, or release.*
	121.[illegible] *Notification of theft, loss, or release.*
	1.20 *Administrative review.*
	121.20 *Administrative review.*

A commenter suggested that APHIS and CDC adopt consistent terminology when referring to biological agents and toxins. The commenter pointed out that the regulations use the following terms: biological agents and toxins, select agents and toxins, overlap agents, and high consequence pathogens.

We agree that APHIS and CDC should use consistent terminology. Therefore, in this final rule, we are removing the terms ''biological agents and/or toxins,'' ''listed agents and/or toxins,'' and ''high consequence livestock pathogens'' each time they appear in 7 CFR part 331 and/or 9 CFR part 121 and adding ''select agents and/or toxins'' in their place. In addition, in 9 CFR part 121, we are removing the term ''overlap agents'' each time it appears and adding ''overlap select agents and/or toxins'' in its place. To reflect this change in terminology, we are also changing the title of both parts from ''Possession, Use, and Transfer of Biological Agents and Toxins'' to ''Possession, Use, and Transfer of Select Agents and Toxins.'' In accordance with these changes, we will be using the term ''select agent and/or toxin'' throughout the preamble of this rule. When it is necessary to specify the type of select agent or toxin, we will use the following terms: ''PPQ select agent and/or toxin'' (for the plant agents and toxins), ''VS select agent and/or toxin'' (for the animal agents and toxins), or ''overlap select agent and/or toxin.'' Unless otherwise specified, the term ''select agent and/or toxin'' will refer to all agents or toxins listed by APHIS.

One commenter stated that APHIS and CDC should harmonize the regulations and provide consistent guidance to entities. This commenter also recommended close collaboration between the agencies for registration, enforcement, and compliance assistance. Another commenter recommended that APHIS and CDC establish one regulatory and reporting mechanism and one office of oougcollab-1.11Tgi67 56.0A.3kjT*reer

Congress has not appropriated any funds to establish such a grant program. Accordingly, we are making no change based on these comments.

One commenter requested that APHIS specify in the final rule that it is the

including the costs of verifying the baseline inventory and the costs of responding to lost vial reports. The commenter estimated that the one-time cost to verify the baseline inventory will be $2 million with recurring costs of about $1 million per year. The commenter also estimated that it will cost about $5 million per year to respond to reports of lost vials of select agents because the response would require, at least, a verification of the inventory.

In response to this comment, the economic analysis in this final rule provides more information about the costs of the inventory recordkeeping requirements. In this final rule, we estimate that it would cost an entity $7,200 to create a baseline inventory (assuming an average of 10 freezers and 3 toxin containers per entity). Assuming that registered entities would have to re-inventory one-half of their freezers each year to maintain an accurate and current inventory, we estimate the total yearly inventory cost for all affected entities to be $274,000. Finally, in the event of a theft or loss, we expect an entity would conduct an inventory of the affected storage freezer or toxin container. We estimate that such an inventory would cost $560 per occurrence.

Interim 7 CFR 331.0 and 9 CFR 121.0 provided that the regulations in each part became effective on February 11, 2003. To minimize the disruption of research or educational projects, both sections also provided additional time for individuals and entities to reach full compliance with the regulations in each part (*i.e.*, a phase-in period). Finally, as established in the November 3, 2003, interim rule, both sections provided for the issuance of provisional certificates of registration and provisional grants of access for individuals under certain conditions.

A number of commenters requested clarification of the provisions for the phase-in period and several commenters requested additional time to comply with certain provisions. Given that all of the dates in 7 CFR 331.0 and 9 CFR 121.0 have passed, the sections are no longer applicable and the issues raised by the commenters are moot. Accordingly, in this final rule, we are removing 7 CFR 331.0 and 9 CFR 121.0.

In 7 CFR 331.1 and 9 CFR 121.1, we define the terms used in the regulations. We are adding definitions of *diagnosis* and *verification* in both sections in this final rule. *Diagnosis* is defined as ''the analysis of specimens for the purpose of identifying or confirming the presence or characteristics of a select agent or toxin provided that such analysis is directly related to protecting the public health or safety, animal health or animal products, or plant health or plant products.'' *Verification* is defined as ''the demonstration of obtaining established performance (*e.g.*, accuracy, precision, and the analytical sensitivity and specificity) specifications for any procedure used for diagnosis.'' In addition, in 9 CFR 121.1, we are amending the definition of *proficiency testing. Proficiency testing* is defined as ''the process of determining the competency of an individual or laboratory to perform a specified test or procedure.'' Finally, we are deleting the definition for *diagnostic laboratory* in both sections and we are deleting the definition for *clinical laboratory* in 9 CFR 121.1. These changes will clarify the exemption provisions and help to ensure that APHIS and CDC consistently apply these provisions.

To be consistent with CDC's definitions, we are adopting CDC's definitions for *HHS Secretary* and *HHS select agent and/or toxin* in 9 CFR 121.1. HHS defined as ''the

laboratory in 9 CFR 121.1. The term does not appear elsewhere in the regulations. Accordingly, we are making no change based on this comment.

A commenter recommended that APHIS define the term ''access'' to mean actual, physical contact with the agent or the realistic opportunity for same.

This issue is addressed below in the sections relating to security risk assessments and security. We are making no change to the definitions in 7 CFR 331.1 or 9 CFR 121.1 based on this comment.

One commenter stated that 9 CFR 121.1 should define the term ''exotic'' so that the term can be removed from the list of agents.

This issue is addressed below in the section relating to the lists of VS and overlap select agents and toxins. Therefore, we are making no change to the definitions in 9 CFR 121.1 in response to this comment.

Interim 7 CFR 331.2 and 9 CFR 121.2 set out the purpose and scope of the regulations. Specifically, 7 CFR 331.2(a) stated that part 331 sets forth the requirements for possession, use, and transfer of biological agents or toxins that have been determined to have the potential to pose a severe threat to plant health or plant products, while 9 CFR 121.2(a) stated that part 121 sets forth the requirements for possession, use, and transfer of biological agents or toxins that have been determined to have the potential to pose a severe threat to both human and animal health, or to animal health or animal products. Both sections noted that the purpose of the regulations is to ensure the safe handling of such agents or toxins, and to protect against the use of such agents or toxins in domestic or international terrorism or for any other criminal purpose.

In this final rule, we are amending both sections to clarify that each part implements the provisions of the Agricultural Bioterrorism Protection Act of 2002. Furthermore, we are amending 9 CFR 121.2 to clarify that overlap select agents and toxins are subject to regulation by both APHIS and CDC.

In interim 7 CFR 331.2 and 9 CFR 121.2, paragraphs (b) and (c) summarized the regulatory requirements. Since these provisions are already set forth in other sections of the regulations, we believe it is unnecessary to summarize them in these sections. Therefore, in this final rule, we are removing paragraphs (b) and (c) fe ws rng m

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have been renamed; thus, *Liberobacter africanus* should be *Candidatus* Liberobacter africanus, and *Liberobacter asiaticus* should be *Candidatus* Liberobacter asiaticus.

We agree. Therefore, in this final rule, we are replacing the entry for *Liberobacter africanus*

disease (VVND) is a velogenic strain. To ensure that we are regulating all of the velogenic strains, in this final rule we are replacing the entry for Newcastle disease virus (VVND) with Newcastle disease virus (velogenic).

A commenter stated the distinction between domestic and exotic vesicular stomatitis virus cannot be justified scientifically. Therefore, it would be more logical to list all vesicular stomatitis viruses except specific viruses that are generally recognized as attenuated (*e.g.*, the VSV-Indiana Lab strain).

We do not believe it is necessary to regulate all strains of vesicular stomatitis virus, especially those strains that have limited morbidity and mortality in the United States. Therefore, we are making no change based on this comment.

Interim 9 CFR 121.3(b) (newly designated § 121.4(b)) listed the biological agents and toxins that have been determined to have the potential to pose a severe threat to both human and animal health, to animal health, or to animal products (overlap select agents and toxins).

Several commenters pointed out that *Clostridium botulinum* is listed in the APHIS regulations but not in the CDC regulations.

APHIS inadvertently listed both *Clostridium botulinum* and Botulinum neurotoxin producing species of *Clostridium* as overlap agents in the December 2002 interim rule. We always intended to only list Botulinum neurotoxin producing species of *Clostridium* in order to be consistent with CDC. Accordingly, we are removing *Clostridium botulinum* from the list of overlap select agents and toxins in this final rule.

A number of commenters argued that overlap agents that are endemic, widespread, and easily isolated from natural sources should not be included in the list of overlap select agents. For these reasons, one commenter recommended that *Francisella tularensis* and *Coxiella burnetii* be removed from the list of overlap agents. Several commenters stated that *Coccidioides immitis* should not be included in the list of overlap select agents because it is endemic in California's Central Valley and is found in many areas of the southwest. Another commenter argued that *Coxiella burnetii* should be removed from the overlap list because ''it is so ubiquitous in nature that its identification as a select agent is meaningless.'' One commenter argued that Eastern equine encephalitis virus should be removed from the overlap list because it is endemic and even if it were intentionally introduced into people, horses, or other domestic animals, there would be little or no chance of spread to cause an adverse agricultural event.

We agree that *Coxiella burnetii, Coccidioides immitis,* and *Francisella tularensis* are endemic, widespread, and easily isolated from natural sources. However, these factors are not sufficient reason to remove these agents from the list of overlap select agents and toxins. Furthermore, we disagree that there is little risk of an adverse agricultural event involving Eastern equine encephalitis virus because it can cause high mortality in horses, and there is no mandatory vaccination program in the United States. We are making no changes based on this comment.

A commenter stated that it is pointless to regulate trichothecenes such as T–2 toxin as select agents if highly toxigenic strains of the toxin-producing organism are not also regulated.

We are regulating T–2 toxin, and not the organism that produces it, because we believe the toxin has the potential to pose a severe threat to public health and safety, to animal health, and to animal products. Accordingly, we are making no change in response to this comment.

Interim 7 CFR 331.3(c)(2), 9 CFR 121.3(c), and 9 CFR 121.3(f)(2) (newly designated 7 CFR 331.3, 9 CFR 121.3, and 9 CFR 121.4) set out the provisions for genetic elements.

One commenter stated there are differences between the APHIS and CDC regulations regarding genetic elements. For example, the regulations seem to imply that no bacterial sequences are regulated, except those from animal agents.

We agree. In the interim regulations, CDC provided that infectious viral sequences of HHS and overlap select agents are regulated, while APHIS provided that infectious viral sequences of overlap agents are regulated and infectious viral and bacterial sequences of PPQ and VS select agents are regulated. To resolve these differences, in this final rule we are adopting CDC's approach for genetic elements. Specifically, newly designated 7 CFR 331.3, 9 CFR 121.3, and 9 CFR 121.4 provide that the following will be considered select agents and toxins:

- Nucleic acids that can produce infectious forms of any of the select agent viruses listed in either 7 CFR part 331 or 9 CFR part 121;
- Recombinant nucleic acids that encode for the functional forms of any toxin listed in either 7 CFR part 331 or 9 CFR part 121 if the nucleic acids: (1) Can be expressed *in vivo* or *in vitro;* or (2) are in a vector or recombinant host genome and can be expressed *in vivo* or *in vitro*; and
- Select agents and toxins listed in either 7 CFR part 331 or 9 CFR part 121 that have been genetically modified.

Another commenter stated that interim 9 CFR 121.3(c) and 121.3(f) conflict—§ 121.3(c) seems to include fragments, while § 121.3(f) exempts them. The commenter pointed out that all genetic elements that cause disease can be fragmented into pieces that cannot cause disease, but that can be reconstituted simply and quickly.

We believe the changes in this final rule will address the differences identified by this commenter. Accordingly, we are making no change based on this comment. However, we note that fragments are not subject to the regulations until reconstituted.

One commenter asked if cDNA is regulated. This commenter also asked how sequence data of select agents will be protected, since it can be used to make a select agent.

A cDNA fragment will be subject to the regulations if it can produce either an infectious form of toxin or a select agent. Sequence data of select agents is already in the public domain, and APHIS cannot protect this information. However, we note that an individual or entity that uses sequence data to produce an infectious agent or toxin will be subject to the select agent regulations. We are making no changes based on this comment.

Interim 7 CFR 331.3(b) and 9 CFR 121.3(e) stated that any biological agent or toxin that is in its naturally occurring environment will not be subject to the requirements of either part, provided that the biological agent or toxin has not been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source.

To be consistent with CDC, we are adopting the phrase ''excluded from the requirements of this part'' in place of the phrase ''will not be subject to the requirements of this part.'' Thus, in this final rule, newly designated 7 CFR 331.3(d)(1), 9 CFR 121.3(d)(1), and 9 CFR 121.4(d)(1) state that a select agent or toxin that is in its naturally occurring environment is excluded from the requirements of the regulations, provided that the agent or toxin has not been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source.

One commenter stated that the naturally occurring environment of a virus is its host. The commenter pointed out that *Coxiella burnetii* can be found in milk samples and asked if the truck moving milk to a processing plant would be subject to the regulations or if

the milk sample submitted to a laboratory for mastitis testing would be subject to the regulations as the milk sample is being collected.

Coxiella burnetii that is contained in milk in a truck or in a diagnostic sample is considered to be in its naturally occurring environment as long as it has not been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source. We are making no changes in response to these comments.

Another commenter stated that the regulations suggest that an agent found in the lymph node of a slaughtered animal (found on histopathology but not cultivated or extracted) is in its naturally occurring environment and, therefore, exempt from notification.

This comment appears to combine the requirements for exclusions and exemptions. A select agent or toxin that has not been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source is considered to be in its naturally occurring environment and, therefore, excluded from the requirements of the regulations. The exemption provisions for overlap select agents and toxins are set forth in newly designated 9 CFR 121.6. Histopathology alone is not a definitive identification of a select agent. However, a select agent that has been identified by a histopathology method that has been validated would need to be reported to APHIS or CDC in accordance with the regulations. We are making no changes in response to this comment.

A commenter stated that any naturally occurring organism expressing a Shigatoxin should be specifically excluded from the list of select agents and toxins.

As previously noted, we are regulating the toxin and not the organisms that produce the toxin. Therefore, it is not necessary to exclude from the requirements of the regulations any naturally occurring organism expressing a Shigatoxin. However, we note that Shigatoxin under the control of a principal investigator, treating physician or veterinarian, or commercial manufacturer or distributor is excluded from the requirements of 9 CFR part 121 if the aggregate amount does not, at any time, exceed 100 mg (newly designated 9 CFR 121.4(d)(3)).

Interim 7 CFR 331.3(c)(1) (newly designated 7 CFR 331.3(d)(2)) provided that nonviable agents that are, bear, or contain listed agents or toxins will not be subject to the requirements of the part because they do not have the potential to pose a severe threat to plant health or plant products. Similarly, interim 9 CFR 121.3(f) (newly designated 9 CFR 121.3(d)(2) and 121.4(d)(2)) provided that nonviable agents or fixed tissues that are, bear, or contain listed agents or toxins will not be subject to the requirements of the part because they do not have the potential to pose a severe threat to both human and animal health, or to animal health or animal products.

In this final rule, we are amending both sections to clarify that these provisions apply to nonviable agents and nonfunctional toxins. These changes will make the provisions in the APHIS and CDC regulations consistent.

A commenter requested clarification of the terms ‘‘nonviable’’ and ‘‘nonfunctional’’ select agents or toxins. The commenter noted that some organisms can survive in nature, others only under lab conditions, and others not under any conditions.

A nonviable agent is not capable of replicating, infecting a plant or animal, or causing disease, while a nonfunctional toxin is not able to produce a toxic effect. These terms are generally understood in the scientific community, and we do not believe that further clarification is needed in the regulations. Therefore, we are making no change in response to this comment.

Footnotes in interim 9 CFR 121.3 stated that the importation and interstate movement of nonviable agents and genetic elements are subject to the permit requirements under 9 CFR part 122.

One commenter asked why a permit is needed for nonviable agents and genetic elements that are excluded from regulation under 9 CFR part 121. The commenter argued that nonviable agents and genetic elements that are not capable of causing disease do not meet the definition of ‘‘organism’’ in part 122. Another commenter requested clarification of the permit requirement for nonviable agents or fixed tissues. The commenter stated that the provision seems to suggest that, for as long as you retain the tissues, you would need to get yearly interstate transport permits even though no further receipt/transport is taking place.

The regulations in 9 CFR part 122 pertain to the movement of organisms and vectors. A nonviable agent or genetic material could serve as a vector of a disease agent through ineffective or insufficient processing methods, and, therefore, require a permit for importation or oxins. These

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seized agent or toxin to an entity eligible to receive such agent or toxin or destroys the agent or toxin by a recognized sterilization or inactivation process;

- The Federal law enforcement agency safeguards and secures the seized agent or toxin against theft, loss, or release and reports any theft, loss, or release of such agent or toxin; and
- The Federal law enforcement agency reports the seizure of the select agent or toxin to APHIS or CDC.

This provision will allow Federal law enforcement agencies to conduct certain law enforcement activities (*e.g.*, collecting evidence from a laboratory crime scene) without being in violation of the regulations. We note, however, that this provision does not authorize the seizure of a select agent or toxin by a Federal law enforcement agency; rather, it establishes the conditions under which a Federal law enforcement agency may seize a select agent or toxin without violating the regulations. Seizure of a select agent or toxin by a Federal law enforcement agency would have to be in accord with that agency's statutory authority.

Interim 7 CFR 331.4, 9 CFR 121.4, and 9 CFR 121.5 (newly designated 7 CFR 331.5, 9 CFR 121.5, and 9 CFR 121.6) set out exemptions.

Interim 9 CFR 121.4(a) provided that clinical or diagnostic laboratories and other entities possessing, using, or transferring overlap agents or toxins that are contained in specimens presented for diagnosis or verification will be exempt from the requirements of part 121, provided that the identification of such agents or toxins is immediately reported to APHIS or CDC, and to other appropriate authorities when required by Federal, State, or local law; and, within 7 days after identification, such agents or toxins are transferred or inactivated, and APHIS Form 2040 is submitted to APHIS or CDC. Interim 7 CFR 331.4(a) and 9 CFR 121.5(a) contained similar exemption provisions for diagnostic laboratories (the term clinical laboratories is not applicable to the plant-related regulations in 7 CFR part 331 or the animal-related regulations in 9 CFR part 121). Exemption provisions for laboratories and other entities that perform proficiency testing were set out in interim 9 CFR 121.4(b) and 121.5(b).

In this final rule, we are amending both parts to clarify the exemption provisions related to clinical or diagnostic laboratories and other entities (for overlap select agents and toxins) and diagnostic laboratories and other entities (for PPQ and VS select agents and toxins). Specifically, paragraph (a) in newly designated 7 CFR 331.5 and paragraphs (a) and (b) in newly designated 9 CFR 121.5 and 121.6 make clear that laboratories and other entities must meet the exemption requirements for each select agent or toxin contained in a specimen that it possesses, uses, or transfers. This change takes into account situations in which a diagnostic laboratory or other entity could be registered for a select agent or toxin but still meet the exemption requirements for other select agents or toxins contained in specimens. We are also amending both parts to clarify that, as a condition of exemption, clinical or diagnostic laboratories and other entities must transfer a select agent or toxin in accordance with the transfer requirements in each part (newly designated 7 CFR 331.16 and 9 CFR 121.16, respectively) or destroy the agent or toxin on-site by a recognized sterilization or inactivation process.

In this final rule, we are also deleting in both parts the requirement that the identification of a select agent or toxin be reported to appropriate authorities when required by Federal, State, or local law (interim 7 CFR 331.4, 9 CFR 121.4, and 9 CFR 121.5). Because this provision merely indicates that additional reporting requirements may exist under Federal, State, or local law, it is not necessary to include this provision in the regulations. It is the entity's responsibility to be familiar with all legal requirements for select agents and toxins.

In addition, newly designated 9 CFR 121.5 and 121.6 require immediate reporting after identification for specified select agents and toxins; identification of the other select agents and toxins must be reported within 7 calendar days after identification. This change will reduce the reporting burden on the public while continuing to provide information that will help us to identify outbreaks and to monitor activities related to select agents and toxins.

Finally, we are deleting footnote 1 in interim 7 CFR 331.4 (newly designated 7 CFR 331.5) because this information is contained in the transfer section in this final rule (newly designated § 331.16). We are also deleting the application and contact information contained in footnotes in interim 7 CFR 331.4, 9 CFR 121.4, and 9 CFR 121.5 because addresses and telephone numbers are subject to change. Information about the submission of forms, notices, and requests for exemptions or exclusions is available on the Internet at *http://www.aphis.usda.gov/programs/ag_selectagent/index/html.*

A commenter asserted that clinical or diagnostic laboratories should be required to secure the agent or toxin prior to transfer or destruction.

We agree. Taking into account the risks posed by select agents and toxins and the security requirements for registered entities, it is reasonable to require that a clinical or diagnostic laboratory or other entity secure the agent or toxin prior to transfer or destruction. Furthermore, we believe it is reasonable to require that a clinical or diagnostic laboratory or other entity report any theft, loss, or release of a select agent or toxin prior to transfer or destruction. Therefore, newly designated 7 CFR 331.5, 9 CFR 121.5, and 9 CFR 121.6 require, as another condition of exemption, that the select agent or toxin be secured against theft, loss, or release during the period between identification of the agent or toxin and transfer or destruction of such agent or toxin, and that any theft, loss, or release of such agent or toxin be reported.

Another commenter argued that the exemptions for clinical and diagnostic laboratories should require, at the very least, that employees of such labs be subject to security risk assessments by the Attorney General.

The Act does not require security risk assessments for employees of entities that are exempt from registration under the regulations (section 212(e)). We believe that the conditions for exemption in this final rule provide adequate safeguard and security measures to protect animal and plant health, and animal and plant products. Accordingly, we are making no change based on this comment.

One commenter requested that APHIS define the term ''identification.'' The commenter asked if a PCR positive reaction constituted identification or simply detection. This commenter also wondered if an entity must report an identification done on a nonviable organism.

If a PCR test is recognized in the scientific community as an identification method, then a result utilizing this test must be reported. If not, reporting is not required. An individual or entity must report an identification done on a nonviable organism in accordance with the regulations. We require this reporting in order to obtain surveillance information about select agents or toxins. We are making no changes in response to this comment.

Several commenters argued that the requirement to transfer an agent or toxin

within 7 calendar days of identification was unrealistic. One commenter stated that delays in transfer approval by APHIS or CDC could result in delays in shipping the samples. Several commenters expressed concern about this deadline due to the unreliability of shippers. Another commenter stated that it is unreasonable and counterproductive to require diagnostic labs to destroy or transfer select agents within 7 days after identification. The commenter said that some labs may process hundreds or thousands of samples each week and generate large numbers of select agent isolates, and transferring these isolates to a qualified lab within 1 week will be very difficult and costly. The commenter claimed that most labs will simply destroy the isolates and that such destruction will result in the loss of valuable scientific material.

Based on information provided by CDC and APHIS' National Veterinary Services Laboratories (NVSL), and taking into consideration the risks posed by select agents and toxins, we believe that 7 days will provide ample time after identification to destroy the agent or toxin, or to make transfer arrangements and to transfer the agent or toxin. However, in this final rule, we are amending newly designated 7 CFR 331.5(a) and 9 CFR 121.5(a) to allow the Administrator to make exceptions to these timeframes, as necessary. We are also amending newly designated 9 CFR 121.6(a) to allow the Administrator or the HHS Secretary to make exceptions to these timeframes for overlap select agents or toxins, as necessary. Finally, we are making similar changes to newly designated 9 CFR 121.5(b) and 9 CFR 121.6(b) to allow for exceptions to the timeframes for proficiency testing, which require that an agent or toxin be transferred or destroyed within 90 calendar days of receipt.

Another commenter recommended a longer holding period for agents and toxins before mandatory inactivation—30 to 45 days instead of 7 days—because the destruction of isolates of select agents after only 7 days is counter to good quality control in labs, which often specifies that isolates and specimens be kept for 30 days, and labs often have cases pending for at least 30 days awaiting additional results. The commenter went on to note that it is good lab practice to maintain the original sample until a case is complete, and labs often maintain samples so that additional testing can be done as needed.

The exemption provisions in interim 7 CFR 331.4(a), 9 CFR 121.4(a), and 9 CFR 121.5(a) (newly designated 7 CFR 331.5(a), 9 CFR 121.5(a), and 9 CFR 121.6(a)) do not require mandatory inactivation of a select agent or toxin. To qualify for an exemption, an individual or entity must satisfy the conditions for exemption, including transferring or destroying the select agent or toxin within 7 calendar days of identification unless directed otherwise by the Administrator or HHS Secretary. However, an individual or entity could continue to hold a select agent or toxin if it registers with APHIS or, for overlap select agents and toxins, if it registers with APHIS and CDC. While we TjTce.Hz

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are produced at USDA diagnostic facilities will be exempt from the requirements of this part.

The regulations (interim 9 CFR 121.4(e); newly designated § 121.6(e)) provide that the Administrator may exempt an individual or entity from the requirements of the part for 30 days if it is necessary to respond to a domestic or foreign agricultural emergency involving an overlap agent or toxin. This exemption may be extended for an additional 30 days.

One commenter argued that the 30-day special exemption granted during an emergency is insufficient to deal with a foreign animal or outbreak emergency. This commenter stated that neither exotic Newcastle disease or the low pathogenic avian influenza outbreaks were resolved in 60 days.

Section 212(g)(1)(D) of the Act sets forth the exemption for agricultural emergencies involving overlap select agents and toxins. The Act specifies that such exemptions may not exceed 60 days. Accordingly, we are making no changes based on this comment.

Interim 7 CFR 331.5, 331.6, and 331.8 and 9 CFR 121.6, 121.7, and 121.9 (newly designated 7 CFR 331.7 and 9 CFR 121.7) set out registration requirements and procedures.

One commenter stated that the regulations do not contemplate or address a situation where an entity has employees that possess, use, or transfer select agents at locations owned and controlled by another entity. The commenter stated that it is a nonprofit organization that provides medical research personnel to Federal agencies. The commenter asserted that the regulations and the registration application should be revised to require registration for the entity that owns or controls the location where agents and toxins are used and stored.

This final rule requires that, unless exempted under the regulations, an individual or entity that possesses, uses, or transfers select agents or toxins must register with APHIS or, for overlap select agents or toxins, APHIS and CDC. The regulations provide for both individuals and entities, even though we expect that most registrants will be entities. Using the example given by the commenter, the Federal agency that possesses, uses, or transfers select agents or toxins would be required to register and restrict access to such agents or toxins to only those individuals approved by the Administrator or HHS Secretary following a security risk assessment by the Attorney General. We are making no change based on this comment.

One commenter requested that USDA and CDC consider a single clearinghouse for registration of select agents. The commenter said the rules require an entity that possesses only human and animal/plant agents (no overlaps) to register separately with each agency; however, this would place an undue burden on the entity by requiring dual registration packages and safety/security plans. Another commenter recommended that APHIS indicate what an entity can do to assist or mitigate conflict between APHIS and CDC on registration applications for overlap agents.

To simplify the registration process and minimize the burden on the public, APHIS and CDC have established a framework by which individuals and entities with various combinations of select agents and toxins may submit their registration applications to either APHIS or CDC. For instance, to apply for a certificate of registration for only PPQ or VS select agents or toxins, or for PPQ and VS select agents or toxins, an individual or entity must submit the registration application package to APHIS. However, to apply for a certificate of registration for overlap select agents or toxins, overlap select agents or toxins and any combination of PPQ or VS select agents or toxins, or HHS select agents or toxins and any combination of PPQ or VS select agents or toxins, an individual or entity must submit the registration application package to APHIS or CDC, but not both. In this final rule, we are amending both sections to set out this new framework for submitting registration applications (newly designated 7 CFR 331.7(d) and 9 CFR 121.7(d)).

As previously discussed, APHIS and CDC are also developing a single shared web-based system that will allow the regulated community to conduct transactions electronically with either agency via a single web portal. By providing a single web portal, APHIS and CDC will be able to interact efficiently and effectively with the regulated community while reducing the burden on the public. We envision that this system will enable the entity to dynamically communicate with APHIS and CDC in a digitally secured environment using a single web portal. The web portal will provide a platform for electronic exchange of information. It will allow entities to access data related to their own registration data and allow them to create, amend, and submit registration applications; requests for approvals for transfers, exemptions, or exclusions; and any other required forms without the need to print, mail, or e-mail hard copies. Hard copy registration materials and other required forms will still be accepted. The single web portal will be available in winter 2005.

Several commenters requested more information about the registration process. One commenter asked how long will it take to receive a certificate of registration after all the paperwork has been submitted. The commenter urged APHIS to promptly process registration applications so as not to disrupt valuable research and impede academic planning. Another commenter suggested that APHIS add information to the final rule to indicate when an entity should submit renewal applications (*i.e.*, at least 90 days prior to expiration).

We are committed to promptly processing initial registration applications and renewal applications. The time needed to process a registration application and issue a certificate of registration depends on the complexity and completeness of the application. However, to provide more guidance about the submission of renewal applications, we recommend that the registration application and the information necessary to conduct the required security risk assessments be submitted at least 8 weeks prior to the expiration of the date of the certificate of registration.

Interim 7 CFR 331.6(b)(1) and 9 CFR 121.7(b)(1) (newly designated 7 CFR 331.7 and 9 CFR 121.7) indicated that, as one of the conditions of registration, the owner or controller of an entity must be approved by APHIS following a security risk assessment by the Attorney General.

A commenter asked who would be deemed to own or control the entity in the context of an academic institution. Another commenter thought the phrase ''individual who controls the facility'' meant the senior administrators to whom the responsible official reports and not the members of the Board of Trustees.

The determination of who is an owner or controller of an academic institution (*i.e.*, institution of higher education) depends on whether it is a public or private institution of higher education. Federal, State, or local governmental agencies, including public institutions of higher education, are exempt from the security risk assessment for the entity and the individual who owns or controls such entity. However, for a private institution of higher education, an individual will be deemed to own or control the entity if the individual is in a managerial or executive capacity with

regard to the entity's select agents or toxins or with regard to the individuals with access to the select agents or toxins possessed, used, or transferred by the entity. We consider an entity to be an institution of higher education if it is an institution of higher education as defined in the Higher Education Act of

requiring in both sections that each individual with access to select agents or toxins have the appropriate education, training, and/or experience to handle or use such agents or toxins (newly designated 7 CFR 331.10(c) and 9 CFR 121.10(c)). However, in this final rule, we are removing the requirement that the responsible official submit information about an individual's training and skills to APHIS (interim 7 CFR 331.10(e) and 9 CFR 121.11(e)). These changes will make it clear that the registered individual or entity, and not APHIS, is responsible for ensuring that an individual with access to select agents or toxins has the appropriate education, training, and/or experience to handle such agents or toxins.

Several commenters argued that access approval should be portable from entity to entity, from location to

hand and be commensurate with the risks posed by the select agent or toxin. We are making no change based on this comment.

One commenter argued that the Attorney General should allow the research community to comment on how the definition of ''restricted person'' will be interpreted and applied. This commenter stated that, while the Attorney General is bound by statutory language in the respective categories, interpretation will be required to make the definitions operational. For instance, the commenter asked if a scientist who has fled political persecution in another country, and who may therefore have an outstanding foreign arrest warrant, would be considered a restricted person. Another commenter recommended that the Administrator reserve the authority, in exceptional circumstances, to allow individuals deemed ineligible to have access to select agents and toxins for a limited time. The commenter stated that it is in the national interest to take a nuanced approach that takes into account the contributions the individual may be able to make to the country. This commenter stated there should be an opportunity for individuals and their sponsoring institutions to make the argument that an individual has exceptional talent and insight that should be used to advance research, and that an individual does not present a security risk, even if he or she meets the criteria for a restricted person.

The statutory requirements are clear, and it is not necessary for the research community to assist in the interpretation and application of the term 'restricted person.' In accordance with the Act, the Administrator may limit or deny access to PPQ and VS select agents and toxins to individuals whom the Attorney General has identified as a ''restricted person'' under 18 U.S.C. 175b. Furthermore, the Administrator must deny access to overlap select agents and toxins to individuals whom the Attorney General has identified as a ''restricted person.'' According to 18 U.S.C. 175b, ''the term ''restricted person'' means an individual who:

- Is under indictment for a crime punishable for a term exceeding 1 year;
- Has been convicted in any court of a crime punishable by imprisonment for a term exceeding 1 year;
- Is a fugitive from justice;
- Is an unlawful user of any controlled substance (as defined in section 102 of the Controlled Substances Act (21 U.S.C. 802));
- Is an alien illegally or unlawfully in the United States;
- Has been adjudicated as a mental defective or has been committed to any mental institution;
- Is an alien (other than an alien lawfully admitted for permanent residence) who is a national of a country as to which the Secretary of State,

purposes specified in the Act. Another commenter stated that toxins should not be subject to the same biocontainment and security measures as viruses, bacteria, fungi, and plant pathogens (which are capable of replication). The commenter suggested a two-tiered approach, with a higher level of security and biocontainment for materials that can be propagated. Similarly, a commenter stated the security requirements should recognize that not all listed agents are equal from a weaponization perspective; therefore, a set of graded protection requirements should be established so that the most dangerous pathogens and the most likely to be weaponized are protected at higher levels than the majority of the select agents.

Because different select agents and toxins pose differing degrees of risk, we believe it would be counterproductive to attempt to prepare a detailed list of prescriptive requirements for entities (*i.e.*, a ''one size fits all'' design standard). Therefore, the regulations contain performance standards for biocontainment/biosafety, security, and incident response that take into account the risks presented by a particular agent or toxin, given its intended use.

With regard to security, newly designated 7 CFR 331.11 and 9 CFR 121.11 require each individual or entity required to register under each part to develop and implement a written security plan. This 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. In addition, newly designated 7 CFR 331.11 and 9 CFR 121.11 require the individual or entity to adhere to specified security requirements or implement measures to achieve an equivalent or greater level of security. We believe these security provisions provide enough flexibility and specificity to allow an individual or entity to develop and implement a security plan that will safeguard the select agent or toxin against unauthorized access, theft, loss, or release.

However, in recognition of the commenters' concerns, we reiterate that APHIS and CDC are working with interagency groups and security experts to draft a document that will provide additional guidance about the security required for select agents and toxins. This document will be available in spring 2005. The 5th edition of the BMBL, which is under development, will provide additional guidance on laboratory security.

Interim 7 CFR 331.11(a)(2)(iii) and 9 CFR 121.12(a)(2)(iii) required that the security plan describe, among other things, cybersecurity.

One commenter recommended that the term cybersecurity be replaced with ''information and cybersecurity.'' The commenter also recommended spelling out the assets that should be protected and how they are to be protected.

In this final rule, we are amending these provisions by removing the word ''cybersecurity'' and adding in its place the words ''information systems control'' (newly designated 7 CFR 331.11(c)(1) and 9 CFR 121.11(c)(1)). This change is consistent with changes made throughout this final rule to ensure that information about select agents and toxins is protected.

Interim 7 CFR 331.11(a)(2)(iv) and 9 CFR 121.12(a)(2)(iv) provided that, with respect to areas containing listed agents or toxins, an entity or individual must adhere to the specified security requirements or implement measures to achieve an equivalent or greater level of security.

Two commenters requested clarification of the term ''area'' with regard to large multi-use laboratories. One commenter stated there is little benefit in terms of security to require access control, specialized training, and personnel background checks for individuals who are only sharing lab space with individuals working with select agents or toxins. Another commenter suggested that the regulations should be flexible enough to allow local solution of this issue (*i.e.*, allowing the entity to designate a portion of the lab as a select agent area for which use and entry restrictions would be governed by the regulations). A commenter recommended that, where security.

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Research Involving Recombinant DNA Molecules.'' Moreover, 7 CFR 331.13 provides that these experiments must be conducted under conditions prescribed by the Administrator, and that the Administrator may revoke approval to conduct these experiments, or suspend or revoke a certificate of registration, if the individual or entity fails to comply with the requirements of that part. A corresponding provision in 9 CFR 121.13 provides for consultation with the HHS Secretary. This has always been the way we have interpreted all of these requirements; however, we are adding these provisions to both sections for clarity.

One commenter stated that the inclusion of the words ''pathogenic trait'' establishes an additional class of experiments that require approval from the Administrator. The commenter recommended that the APHIS and CDC requirements be identical.

We agree. Accordingly, we are deleting the words ''pathogenic trait'' in both sections of this final rule (newly designated 7 CFR 331.13(a)(1) and 9 CFR 121.13(a)).

One commenter stated that the regulations should be amended to refer to the NIH Guidelines rather than list the types of experiments that are restricted in the regulations. The commenter noted that the NIH Guidelines are subject to change and the regulations would not be as current as the guidelines and more difficult to amend, if necessary.

One of the reasons APHIS included these provisions in the regulations was to ensure that these categories of experiments are conducted only if safe to do so. By including these provisions in the regulations, we are providing notice to the public and establishing enforceable regulatory requirements. APHIS would have difficulty enforcing the provisions of the NIH Guidelines. If it becomes necessary to revise the list of restricted experiments, we will initiate rulemaking and provide notice and opportunity for public comment. For these reasons, we are making no change based on this comment.

A commenter suggested that the NIH

while interim 9 CFR 121.13 (newly designated § 121.15) required the responsible official to provide appropriate training in biosafety, containment, and security procedures to all individuals with access to listed agents and toxins. Both sections required the responsible official to provide information and training to an individual at the time the individual is assigned to work with a listed agent and toxin, and to provide refresher training annually.

A commenter requested clarification about the training requirements. This commenter wondered what would be considered appropriate training, what qualifications an individual would need to train others, and who decides if the training is adequate. Another commenter recommended that APHIS revise the training provisions to require training for approved individuals working with select agents and toxins and unapproved individuals working in or visiting areas where select agents and toxins are handled or stored. The commenter suggested that such training may be modified according to the needs of the individual, the work they will do, and their potential exposure. A commenter noted that APHIS' training requirements cover fewer staff than CDC's training requirements (*i.e.*, only those individuals handling the agents or toxins). The commenter recommended that the APHIS and CDC requirements be consistent.

In response to these comments, in this final rule we are amending both sections to require that an individual or entity provide information and training on

assess the biosafety and security requirements. The commenter also asked what standards will be used by the inspectors to assess compliance with the regulations.

APHIS inspectors will have the appropriate training and security clearances (at least a security risk assessment) to inspect and evaluate an entity's premises and records to ensure compliance with the regulations. APHIS inspectors will use the standards established in the regulations and published guidelines (*e.g.*, BMBL) to determine compliance. While we expect that, normally, only one inspector will be needed to conduct an inspection, occasionally more than one inspector may be needed to evaluate an entity's biosafety, containment, and security.

APHIS and CDC will coordinate inspections to minimize the burden on the entity. This coordination will ensure that inspections by APHIS and CDC are not duplicative. However, additional inspections may be required under certain circumstances. For instance, another inspection may be required for amendments to a certificate of registration (*e.g.*, addition of a laboratory) or to satisfy APHIS' permit requirements.

Interim 7 CFR 331.16(a) and 9 CFR 121.17(a) required the responsible official to orally notify APHIS and appropriate Federal, State, or local law enforcement agencies immediately upon discovery of a theft or loss of listed agents or toxins. We also required that the oral notification be followed by a written report within 7 days. In this final rule, newly designated 7 CFR 331.19(a) and 9 CFR 121.19(a) provide that thefts or losses must be reported to APHIS or CDC. In addition, these paragraphs clarify that thefts or losses must be reported even if the select agent or toxin is subsequently recovered or the responsible parties are identified. These changes will make the APHIS and CDC regulations consistent. Finally, we are specifying the information that must be reported to APHIS or CDC (newly designated 7 CFR 331.19(a) and 9 CFR 121.19(a)). We believe this change will clarify the requirements for notification of theft or loss of select agents and toxins.

Interim 7 CFR 331.16(b) and 9 CFR 121.17(b) provided that the responsible official must orally notify APHIS immediately upon discovery that a release of a listed agent or toxin has occurred outside the biocontainment area. We also required that the oral notification of a release be followed by a written report within 7 days. The regulations further provided that APHIS will notify relevant Federal, State, and local authorities, and the public, if necessary. In § 121.17(b), we additionally provided that, if the release involves an overlap agent or toxin, we will also notify the Secretary of Health and Human Services.

In this final rule, newly designated 7 CFR 331.19(b) requires that APHIS or CDC be notified immediately upon discovery of a release of a PPQ select agent or toxin outside the primary barriers of the biocontainment area while 9 CFR 121.19(b) requires that APHIS or CDC be notified immediately upon discovery of a release of a VS or overlap select agent or toxin causing occupational exposure or a release outside the primary barriers of the biocontainment area. The requirement for notification of a release outside of the primary barriers of the biocontainment area is a clarification. This is how we have always interpreted the provision regarding release outside the biocontainment area; however, we are making this change to make it clear to the public. In 9 CFR 121.19(b), we are adding the provision for occupational exposure to be consistent with CDC's regulations. We did not include this provision in 7 CFR 331.19 because 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. In both sections, we are also specifying the information that must be reported to APHIS or CDC. We believe these changes will clarify the requirements for notification of a release.

Finally, we are deleting the provision that APHIS will notify relevant Federal, State, and local authorities, and the public in the event a release poses a threat to animal health or animal products. This is an administrative action taken by APHIS and it is unnecessary to include this information in the regulations.

A commenter requested clarification of the term ''unintentional release.'' The commenter stated that it can be interpreted to include any exposure or release at any biosafety level.

The term ''unintentional release'' is not used in either the interim regulations or this final rule. Therefore, we are making no change based on this comment.

Several commenters urged APHIS to exempt from notification those accidents (*i.e.*, releases) that take place entirely within biosafety labs where the select agent is being handled at the appropriate biosafety level. One commenter went on to state that an exposed worker may be so concerned

agents or toxins to appeal that decision (interim 7 CFR 331.17 and 9 CFR 121.18; newly designated 7 CFR 331.20 and 9 CFR 121.20). However, in accordance with the Act, an entity may not appeal the denial or limitation of an individual's access to select agents or toxins. The regulations do not provide exemptions for research. However, we note that an individual's access to PPQ select agents or toxins and VS select agents or toxins may be limited or denied if an individual is a restricted person under 18 U.S.C. 175b. In addition, an individual's access to PPQ select agents or toxins, VS select agents or toxins, or overlap select agents or toxins may be limited or denied if an individual is reasonably suspected by any Federal law enforcement or intelligence agency of committing a crime set forth in 18 U.S.C. 2332b(g)(5), knowing involvement with an organization that engages in domestic or international terrorism (as defined in 18 U.S.C. 2331) or with any other organization that engages in intentional crimes of violence, or being an agent of a foreign power as defined in 50 U.S.C. 1801. For these reasons, we are making no changes based on this comment.

We are also making minor, nonsubstantive changes to the

[1] Any microorganism (including, but not limited to, bacteria, viruses, fungi, rickettsiae, or protozoa), or infectious substance, or any naturally occurring, bioengineered, or synthesized component of any such microorganism or infectious substance, capable of causing: (1) Death, disease or other biological malfunction in a human, an animal, a plant, or another living organism; (2) deterioration of food, water, equipment, supplies, or material of any kind; or (3) deleterious alteration of the environment.

[2] The toxic material or product of plants, animals, microorganisms (including, but not limited to, bacteria, viruses, fungi, rickettsiae, or protozoa), or infectious substances, or a recombinant or synthesized molecule, whatever their origin and method of production, and includes: (1) Any poisonous substance or biological product that may be engineered as a result of biotechnology produced by a living organism; or (2) any poisonous isomer or biological product, homolog, or derivative of such a substance.

also incur costs associated with eradication and quarantine enforcement to prevent further spread, and in the case of intentional introduction—law enforcement. In addition, there is the potential for a disruption in the domestic food supply, whether through contamination, consumer perception, or both. Past food safety incidents have shown that consumer perceptions (both domestic and international) about an implicated food product and about the producing country or sector's ability to produce safe food are slow to recover and can have a lasting influence on food demand and global trade.[3] As such, the benefits associated with the rule are the avoided losses to the animals or plants that could be attacked by these organisms, and their products and markets.

The costs associated with outbreaks can be very high as is demonstrated by natural outbreaks associated with select agents that have occurred. For example, it has been estimated that the losses to agriculture and the food chain from the recent foot-and-mouth disease (FMD) outbreak in the United Kingdom (UK), including the costs compensated by the government, amount to about £3.1 billion ($4.7 billion). In 1999, it was estimated that the potential impacts of an FMD outbreak in California alone would be between $8.5 and $13.5 billion.[4] Also, a bovine spongiform encephalopathy (BSE) crisis occurred in the UK (which has a cattle industry about one-tenth the size of that in the United States) in 1996. It has been estimated [5] that the total resource costs to the UK economy as a result of BSE in the first 12 months after the onset of the 1996 crisis were in the range of £740 million to £980 million ($1.2 billion to $1.5 billion), or just over 0.1 percent of the gross domestic product of the United Kingdom. In addition to these losses, the UK lost its entire export market for beef following the crisis.

The above cited consequences relate to natural or accidental introduction. Deliberate introduction greatly increases the probability of an agent or toxin becoming established and causing wide-ranging and devastating impacts on the economy, disruption to society, diminished confidence in public and private institutions, and possible loss of life. The perpetrators would have the advantage of controlling the time of introduction of the agent, introducing agents into remote or highly susceptible areas, multiple introductions of the same agent, or simultaneous release of different agents. Intentional introductions permit an increased probability of survival of a pathogen, the use of highly virulent strains and high concentrations of inoculum, and precise timing of release to coincide with maximal colonization potential.[6]

The rule is intended to ensure that any entity that possesses, uses or transfers a select agent or toxin is registered and has safeguard, containment, and disposal requirements that are commensurate with the risk of that agent or toxin. Affected entities vary widely, and therefore, the biosafety/biocontainment, incident response and physical security situation will vary widely from one entity to another, as will the specific changes that will need to occur at a given entity to comply with this rule.

Entities that possess, use, or transfer

[3] Buzby, J.C. *Effects of food-safety perceptions on food demand and global trade.* Changing Structure of Global Food Consumption and Trade/WRS–01–1. Economic Research Service/USDA.

[4] Ekboir, J.M. *Potential impact of foot-and-mouth disease in California: the role and contribution of animal health surveillance and monitoring services.* Davis, CA: Agricultural Issues Center, Division of Agriculture and Natural Resources, University of California, Davis, 1999.

[5] DTZ Pieda Consulting. *Economic Impact of BSE on the UK economy.* A Report commissioned by the UK Agricultural Departments and HM Treasury.

[6] National Research Council.

[7] Those entities for which the CDC is considered the primary regulatory agency are considered in conjunction with the CDC rule.

[8] Thus far, APHIS has received 148 applications for registration or exemption. Of those, 72 were exempt, have been shifted to CDC, been withdrawn, or denied.

they wish to become exempt. Thus far, APHIS has received 34 exemption applications, and anticipates receiving an additional one per year. It is estimated that applying for an exemption requires 1.17 hours (0.17 managerial hours at $86.09 per hour [9], and 1 technical hour at $69.34 per hour), or $84 per exemption application. Based on the number of exemption applications received, the total initial cost is estimated to have been $2,900, while the yearly cost for new applicans5tal initial

[9] For purposes of this analysis we use estimates of an average hourly respondent labor rate (including fringe and overhead) of $86.09 for managerial staff, and $69.34 for technical staff. Based on the 2000 Occupational Employment Statistics Survey, Bureau of Labor Statistics.

[10] Based on information from the registration applications, 40 percent of the registered entities have 1 PI, 30 percent have 2 PIs, 11 percent have 3 PIs, 6 percent have 4 PIs, 3 percent have 5 PIs, 3 percent have 6 PIs, 3 percent have 7 PIs, and 1 percent have 9 PIs.

[11] To minimize the administrative burden associated with this new registration program, initially APHIS will assign expiration dates ranging from 24 to 36 months to stagger the dates for renewing registration. Upon renewal, it is expected that all certificates of registration will be valid for 3 years.

12

management, but not biometric technology. The cost per square foot assumes single story entities and has been adjusted for laboratory type entities. For buildings under 80,000 ft2 the average cost/ft^2 is $8.71. In addition, there is an adjustment factor for retrofitting existing buildings. It should be noted that for very small entities, the cost/ft^2 can be considerably higher.[15] It should also be noted that these costs per ft^2 are based on security installations of state-of-the-art technology. In addition to the entity security assessment and access control discussed above, a given entity could need none, some, or all of the following to maintain its physical security. Entry control equipment includes x-ray—small unit ($28,000 per unit), x-ray—large unit ($40,000 per unit), and metal detector(s) ($20,000 per unit). Other features would entail yearly recurring costs. Off-site monitoring ($10,000 to $45,000 per year); an equipment maintenance agreement ($12,000 to $30,000 per year); and guard service—unarmed ($30.00/hr per security post), armed ($35.00/hr per security post), and a supervisor ($40.00/hr).[16] Following September 11, 2001, more comprehensive security packages have been (or will be) added to APHIS facilities including many of these additional features. There are, however, alternatives to the specific services that can greatly reduce costs and could be acceptable depending on the security needs of a given entity, *e.g.,* remote monitoring and response to alarms instead of on-site guard service. Also, an entity may have some or all of the services already included in an overall facility operational and maintenance plan. An example would be a laboratory holding select agents or toxins that is part of an academic institution where support services are already incurred by the academic institution, *e.g.,* campus police for security response.

Because security needs are site-specific and the rule allows for site-specific security solutions, the approaches and applications will be varied. The above physical security components, and others, may have to be added in various quantities (including none) to meet the specific security needs of an entity. The entities covered in this rule can and do vary from a small laboratory contained within a larger facility to large dedicated buildings to large groups of buildings and land. Small laboratories in larger buildings are unlikely to need access controlled gates, a security fence, or even guard service (although a university or commercial entity may already have a security force which would be considered in assessing security needs). Larger entities will inevitably have more and different security needs than small ones. These entities naturally have more points of access and are more likely to need features such as fences or gates to control access. In addition, the costs themselves are very site specific; there can be literally hundreds of variables that will influence cost at a specific site. The variation begins with the needs of the individual entity (views of which can differ from administration, scientist, and physical security points of view) and is influenced by the characteristics of the site—for example, linked areas are in different buildings, on opposite sides of a fire wall, etc. Generally labor for installation (approximately $96/hour in Washington, DC for installation work on electronic access control)[17] is the most expensive and variable cost of these systems.

A review of 20 security plans of registered entities gives an indication of the nature of security present at affected entities. It also gives an indication of the nature of improvements to security that have occurred since the implementation of the interim rule, or are planned, or will need to occur at affected entities. All showed a good base of security. In fact, a number require no improvement under this rule. Improvements that have already occurred or have been recommended include installing intrusion detection systems, installing or expanding CCTV surveillance, card-key access control and standard locks. Often an entity's standard operating procedures for security sufficiently serve in place of a limited number or lack of electronic controls. Because

17

[15] Equivalent security needs at two buildings can have significant differences in cost per ft^2. For example, the need for one $1000 video camera would add $1 to the ft^2 cost of a 1000 ft^2 facility, but only $0.1 to a 10,000 ft^2 one.

[16] Robert Rice, Security Manager, APHIS select agent program.

[17] Christian Lee, Physical Security Specialist, USDA–APHIS–FMD–ESB. Personal communication.

[18] Based on a review of 20 security plans for select agents or toxins submitted to APHIS. The review covered a broad spectrum of security plans, and type of entity. Plans were reviewed at random. Robert Rice, Security Manager, APHIS select agent program.

[19] Among others: Presidential Decision Directive 63, Critical Infrastructure Protection; the Computer Security Act of 1987 (Public Law (PL) 100–235); the Computer Fraud and Abuse Act (18 U.S.C. Sec. 1030 [1993]); Office of Management and Budget (OMB) Circular No. A–123, Management Accountability and Control; Appendix III of OMB Circular No. A–130, Management of Federal Information Resources; FED–STD–1037A, ''An Electronic Means for Communicating Information; and the Electronic Communications Privacy Act (18 U.S.C. 2701).

[20] The average number of individuals needing security risk assessments per entity.

and 3 toxin containers at a given registered entity, it would cost $7,200 per entity to create this baseline inventory. Based on 76 registered entities, the baseline inventory would cost a total of $548,000. The inventory will have to be verified periodically. Assuming that the registered entities would have to re-inventory one-half of their freezers each year to maintain an accurate and current inventory, yields a yearly inventory cost of $274,000.

Other record keeping includes copies of the biosafety/biocontainment, security and incident response plans, a list of individuals with access to select agents and toxins, training records, inventory records, permits and transfer documents, security records, and incident reports. It is estimated that complying with the record keeping requirements will require 10 hours per PI (3 managerial and 7 technical hours per PI), between 10 and 90 hours per entity per year or $745 to $6,700 per entity. The total cost of yearly record keeping is estimated to be $132,000 based on the current number of affected entities, and the number of PIs at those entities.

The rule also requires oral notification immediately upon discovery of the theft or loss of select agents or toxins,

[21] 1997 Economic Census. Department of Commerce, Census Bureau.

[22] AAVLD provided information on 10 veterinary diagnostic laboratories. These laboratories ranged in size form 11 to 100 employees including faculty, staff (part- and full-time), and students. In addition, the AAVLD president estimated that diagnostic laboratories in general would likely have between 6 and 80 employees. According to Dr. Denise Spenser, USDA–APHIS, university research on select agents likely involves fewer than 100 individuals (3 to 5 principal investigators out of about 25 faculty members in each of 3 or 4 departments—microbiology (veterinary microbiology), chemistry, and physiology, 3 to 5 (20 at most) investigators, technicians, and students in each laboratory).

[23] Based on a review of 20 security plans of affected entities.

[24] The baseline estimated cost/ft^2 of $8.71/ft^2 for facilities less than 30,000 ft2 in size, plus an adjustment of 17.7% for retrofitting existing structures.

25

Manufacturing,'' and NAICS 325414, ''Biological Product (except Diagnostic) Manufacturing.''

The Small Business Administration (SBA) has established guidelines for determining when establishments are to be considered small under the Regulatory Flexibility Act. An entity in NAICS 541710, 325413 or 325414 is considered small with 500 or fewer employees, in 325412 with 750 or fewer employees. An entity in NAICS 611310 is considered small with annual receipts/revenues of $6 million or less.

While the establishment size breakdown in the Economic Census does not precisely fit the SBA guidelines, it still shows that the vast majority (more than 90 percent) of life sciences research & development establishments can be considered small. More than 99 percent of biological (except diagnostic) manufacturing, more than 98 percent of diagnostic manufacturing, and at least 94 percent of pharmaceutical manufacturing are considered small. The economic census does not contain information on the establishment size of veterinary service entities. According to data from the U.S. Department of Education, about 31 percent of reporting postsecondary institutions had revenue of less than $6 million in fiscal year 1995–96.[26]

Based on the available information, this rule is not anticipated to have a substantial impact on a significant number of small entities.

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This rule has been prompted by the need to prevent the misuse of select agents and toxins and thereby reduce the potential for those pathogens to harm humans, animals, animal

[26] IPEDS.

(1) Nucleic acids that can produce infectious forms of any of the select agent viruses listed in paragraph (b) of this section.

(2) Recombinant nucleic acids that encode for the functional forms of any toxin listed in paragraph (b) of this section if the nucleic acids:

(i) Can be expressed *in vivo* or *in vitro*; or

(ii) Are in a vector or recombinant host genome and can be expressed *in vivo* or *in vitro.*

(3) Select agents and toxins listed in paragraph (b) of this section that have been genetically modified.

(d) Select agents or toxins that meet any of the following criteria are excluded from the requirements of this part:

(1) Any select agent or toxin that is in its naturally occurring environment, provided that the agent or toxin has not been intentionally introduced,

[1] These conditions may apply to more than one individual.

entity's select agents or toxins or with regard to the individuals with access to the select agents or toxins possessed, used, or transferred by the entity.

(ii) For entities other than institutions of higher education, an individual will be deemed to own or control the entity if the individual:

(A) Owns 50 percent or more of the entity, or is a holder or owner of 50 percent or more of its voting stock; or

(B) Is in a managerial or executive capacity with regard to the entity's select agents or toxins or with regard to the individuals with access to the select agents or toxins possessed, used, or transferred by the entity.

(4) An entity will be considered to be an institution of higher education if it is an institution of higher education as defined in section 101(a) of the Higher Education Act of 1965 (20 U.S.C. 1001(a)), or is an organization described in 501(c)(3) of the Internal Revenue Code of 1986, as amended (26 U.S.C. 501(c)(3)).

(5) To obtain a security risk assessment, an individual or entity must submit the information necessary to conduct a security risk assessment to the Attorney General.

(d) To apply for a certificate of registration for only PPQ select agents or toxins, or for PPQ and VS select agents or toxins, an individual or entity must submit the information requested in the registration application package (APHIS/CDC Form 1) to APHIS. To apply for a certificate of registration for overlap select agents or toxins, overlap select agents or toxins and any combination of PPQ or VS select agents or toxins, or HHS select agents or toxins and any combination of PPQ or VS select agents or toxins, an individual or entity must submit the information requested in the registration application package (APHIS/CDC Form 1) to APHIS or CDC, but not both.

(e) Prior to the issu4nce of a certificate of registration, the responsible official must promptly provide notification of any changes to the application for registration by submitting the relevant page(s) of the registration application.

(f) The issu4nce of a certificate of registration may be contingent upon inspection or submi303on of additional information, such as the security plan, biosafety plan, incident response plan, or any other documents required to be prepared under this part.

(g) A certificate of registration will be valid for one physicefalocation (a room, a building, or a group of buildings) where the responsible official will be able to perform the responsibilities required in this part, for specific select agents or toxins, and for specific activities.

(h) A certificate of registration may be amended to reflect changes in circumae4nces (*e.g.*, replacement of the responsible official or other personnel changes, changes in ownership or control of the entity, changes in the activities involving any select agents or toxins, or the addition or removal of select agents or toxins).

(1) Prior to any change, the responsible official must apply for an amendment to a certificate of registration by submitting the relevant page(s) of the registration application.[2]

(2) The responsible official will be notified in writing if an application to amend a certificate of registration has been approved. Approval of an amendment may be contingent upon an inspection or submi303on of additional information, such as the security plan, biosafety plan, incident response plan, or any other documents required to be prepared under this part.

(3) No change may be made without such approval.

(i) An entity must immediately notify APHIS or CDC if it loses the services of its responsible official. In the event that an entity loses the services of its responsible official, an entity may continue to possess or use select agents or toxins only if it appoints as the responsible official another individual who has been approved by the Administrator or the HHS Secretary following a security risk assessment by the Attorney General and who meets the requirements of this part.

(j) A certificate of registration will be terminated upon the written request of the entity if the entity no longer possesses or uses any select agents or toxins and no longer wishes to be registered.

(k) A certificate of registration will be valid for a maximum of 3 years.

331.8 [illegible]

(a) An application may be denied or a certificate of registration revoked or suspended if:

(1) The individual or entity, the responsible official, or an individual who owns or controls the entity is within any of the categories described in 18 U.S.C. 175b;

(2) The individual or entity, the responsible official, or an individual who owns or controls the entity is reasonably suspected by any Federal law enforcement or intelligence agency of:

(i) Committing a crime set forth in 18 U.S.C. 2332b(g)(5); or

(ii) Knowing involvement with an organization that engages in domestic or international terrorism (as defined in 18 U.S.C. 2331) or with any other organization that engages in intentional crimes of violence; or

(iii) Being an agent of a foreign power as defined in 50 U.S.C. 1801;

(3) The individual or entity does not meet the requirements of this part; [3] or

(4) It is determined that such action is necessary to protect plant health or plant products.

(b) Upon revocation or suspen03on of a certificate of registration, the individual or entity must:

(1) Immediately stop all use of each select agent or toxin covered by the revocation or suspen03on order;

(2) Immediately safeguard and secure each select agent or toxin covered by the revocation or suspen03on order from theft, loss, or release; and

(3) Comply with all disposition instructions issued by the Administrator for each select agent or toxin covered by the revocation or suspen03on.

(c) Denial of an application for registration and revocation or suspen03on of registration may be appealed under § 331.20. However, any denial of an application for registration or revocation or suspen03on of a certificate of registration will remain in effect until a final agency deci03on has been rendered.

331. [illegible]

(a) An individual or entity required to register under this part must designate an individual to be the responsible official. The responsible official must:

(1) Be approved by the Administrator or the HHS Secretary following a security risk assessment by the Attorney General;

[2] Depending on the change, a security risk assessment by the Attorney General may also be required (*e.g.*, replacement of the responsible official, changes in ownership or control of the entity, new researchers or graduate students, etc.).

[3] If registration is denied for this reason, we may provide technicefaa303ae4nce and guidance.

responsible official, who may act for the responsible official in his/her absence. These individuals must have the authority and control to ensure compliance with the regulations when acting as the responsible official.

(c) The responsible official must report the identification and final disposition of any select agent or toxin contained in a specimen for diagnosis or verification.

(1) The identification of the select agent or toxin must be immediately reported by telephone, facsimile, or e-mail. The final disposition of the agent or toxin must be reported by submission of APHIS/CDC Form 4 within 7 calendar days after identification. A copy of the completed form must be maintained for 3 years.

(2) Less stringent reporting may be required during agricultural emergencies or outbreaks, or in endemic areas.

§ 331.10 [illegible]

(a) An individual or entity required to register under this part may not provide an individual access to a select agent or toxin, and an individual may not access a select agent or toxin, unless the individual is approved by the Administrator or the HHS Secretary following a security risk assessment by the Attorney General.

(b) An individual will be deemed to have access at any point in time if the individual has possession of a select agent or toxin (*e.g.*, carries, uses, or manipulates) or the ability to gain possession of a select agent or toxin.

(c) Each individual with access to select agents or toxins must have the appropriate education, training, and/or experience to handle or use such agents or toxins.

(d) To apply for access approval, each individual must submit the information necessary to conduct a security risk assessment to the Attorney General.

(e) An individual's security risk assessment may be expedited upon written request by the responsible official and a showing of good cause (*e.g.*, agricultural emergencies, national security, or a short-term visit by a prominent researcher). A written decision granting or denying the request will be issued.

(f) An individual's access approval may be denied, limited, or revoked if:

(1) The individual is within any of the categories described in 18 U.S.C. 175b;

(2) The individual is reasonably suspected by any Federal law enforcement or intelligence agency of committing a crime set forth in 18 U.S.C. 2332b(g)(5); knowing involvement with an organization that engages in domestic or international terrorism (as defined in 18 U.S.C. 2331) or with any other organization that engages in intentional crimes of violence; or being an agent of a foreign power as defined in 50 U.S.C. 1801; or

(3) It is determined that such action is necessary to protect plant health or plant products.

(g) An individual may appeal the Administrator's decision to deny, limit, or revoke access approval under § 331.20.

(h) Access approval is valid for a maximum of 5 years.

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

[5] For guidance, see the NIH publication, ''NIH Guidelines for Research Involving Recombinant DNA Molecules.'' This document is available on the Internet at *http://www.aphis.usda.gov/programs/ag_selectagent/index.html.*

[6] Nothing in this section is meant to supersede or *IH*

(i) Has at the time of transfer a certificate of registration that covers the particular select agent or toxin to be transferred and meets all the requirements of this part;

(ii) Meets the exemption requirements for the particular select agent or toxin to be transferred; or

(iii) Is transferring the select agent or toxin from outside of the United States and meets all import requirements.

(2) At the time of transfer, the recipient has a certificate of registration that includes the particular select agent or toxin to be transferred and meets all of the requirements of this part.

(c) On a case-by-case basis, the Administrator may authorize a transfer of a select agent or toxin not otherwise eligible for transfer under this part under conditions prescribed by the Administrator.

(d) To obtain authorization for a transfer, APHIS/CDC Form 2 must be submitted.

(e) The recipient must submit a completed APHIS/CDC Form 2 within 2 business days of receipt of a select agent or toxin.

(f) The recipient must immediately notify APHIS or CDC if the select agent or toxin has not been received within 48 hours after the expected delivery time or if the package containing the select agent or toxin has been damaged to the extent that a release of the select agent or toxin may have occurred.

(g) An authorization for a transfer shall be valid only for 30 calendar days after issuance, except that such an authorization becomes immediately null and void if any facts supporting the authorization change (*e.g.*, change in the certificate of registration for the sender or recipient, change in the application for transfer).

(h) The sender must comply with all Rzatrduireatioe.g.

(v) The location (building, room) from which the release occurred; and

(vi) The number of individuals potentially exposed at the entity;

(vii) Actions taken to respond to the release; and

[9] An entity may not appeal the denial or limitation of an individual's access to select agents or toxins.

to animal health, or to animal products. Overlap select agents and toxins are subject to regulation by both APHIS and CDC.

121.3

(a) Except as provided in paragraphs (d) and (e) of this section, the Administrator has determined that the biological agents and toxins listed in this section have the potential to pose a severe threat to animal health or to animal products.

(b) VS select agents and toxins:

African horse sickness virus;

African swine fever virus;

Akabane virus;

Avian influenza virus (highly pathogenic);

Bluetongue virus (exotic);

Bovine spongiform encephalopathy agent;

Camel pox virus;

Classical swine fever virus;

Cowdria ruminantium (Heartwater);

Foot-and-mouth disease virus;

Goat pox virus;

Japanese encephalitis virus;

Lumpy skin disease virus;

Malignant catarrhal fever virus (Alcelaphine herpesvirus type 1);

Menangle virus;

Mycoplasma capricolum/*M.* F38/*M. mycoides capri* (contagious caprine pleuropneumonia);

Mycoplasma mycoides mycoides (contagious bovine pleuropneumonia);

Newcastle disease virus (velogenic);

Peste des petits ruminants virus;

Rinderpest virus;

Sheep pox virus;

Swine vesicular disease virus;

Vesicular stomatitis virus (exotic).

(c) Genetic elements, recombinant nucleic acids, and recombinant organisms:

(1) Nucleic acids that can produce infectious forms of any of the select agent viruses listed in paragraph (b) of this section.[1]

(2) Recombinant nucleic acids that encode for the functional forms of any toxin listed in paragraph (b) of this section if the nucleic acids:

(i) Can be expressed *in vivo* or *in vitro;* or

(ii) Are in a vector or recombinant host genome and can be expressed *in vivo* or *in vitro.*

(3) VS select agents and toxins listed in paragraph (b) of this section that have been genetically modified.

(d) VS select agents or toxins that meet any of the following criteria are excluded from the requirements of this part:

(1) Any VS select agent or toxin that is in its naturally occurring environment, provided that the agent or toxin has not been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source.

(2) Nonviable VS select agents or nonfunctional VS toxins.[2]

(e) An attenuated strain of a VS select agent or toxin may be excluded from the requirements of this part based upon a determination that the attenuated strain does not pose a severe threat to animal health or to animal products.

(1) To apply for an 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 of the applicant. Exclusions will be published periodically in the notice section of the and will be listed on the Internet at *http://www.aphis.usda.gov/programs/ag_selectagent/index.html.*

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

(3) An individual or entity may make a written request to the Administrator for reconsideration of a decision denying an exclusion application. The written request for reconsideration must state the facts and reasoning upon which the individual or entity relies to show the decision was incorrect. The Administrator will grant or deny the request for reconsideration as promptly as circumstances allow and will state, in writing, the reasons for the decision.

(f) Any VS select agent or toxin seized by a Federal law enforcement agency will be excluded from the requirements of this part during the period between seizure of the agent or toxin and the transfer or destruction of such agent or toxin provided that:

(1) As soon as practicable, the Federal law enforcement agency transfers the seized agent or toxin to an entity eligible to receive such agent or toxin or destroys the agent or toxin by a recognized sterilization or inactivation process.

(2) The Federal law enforcement agency safeguards and secures the seized agent or toxin against theft, loss, or release, and reports any theft, loss, or release of such agent or toxin.

(3) The Federal law enforcement agency reports the seizure of the select agent or toxin to APHIS or CDC.

(i) The seizure of any of the following VS select agents and toxins must be reported within 24 hours by telephone, facsimile, or e-mail: African horse sickness virus, African swine fever virus, avian influenza virus (highly pathogenic), bovine spongiform encephalopathy agent, classical swine fever virus, foot-and-mouth disease virus, Newcastle disease virus (velogenic), rinderpest virus, and swine vesicular disease virus. This report must be followed by submission of APHIS/CDC Form 4 within 7 calendar days after seizure of the select agent or toxin.

(ii) For all other VS select agents or toxins, APHIS/CDC Form 4 must be submitted within 7 calendar days after seizure of the agent or toxin.

(iii) A copy of APHIS/CDC Form 4 must be maintained for 3 years.

(4) The Federal law enforcement agency reports the final disposition of the select agent or toxin by submission of APHIS/CDC Form 4. A copy of the completed form must be maintained for 3 years.

121.4

(a) Except as provided in paragraphs (d) and (e) of this section, the Administrator has determined that the biological agents and toxins listed in this section have the potential to pose a severe threat to public health and safety, to animal health, or to animal products.

(b) Overlap select agents and toxins:

Bacillus anthracis;

Botulinum neurotoxins;

Botulinum neurotoxin producing species of *Clostridium;*

Brucella abortus;

Brucella melitensis;

Brucella suis;

Burkholderia mallei;

Burkholderia pseudomallei;

Clostridium perfringens epsilon toxin;

Coccidioides immitis;

Coxiella burnetii;

Eastern equine encephalitis virus;

Francisella tularensis;

Hendra virus;

Nipah virus;

Rift Valley fever virus;

Shigatoxin;

Staphylococcal enterotoxins;

T–2 toxin;

Venezuelan equine encephalitis virus.

(c) Genetic elements, recombinant nucleic acids, and recombinant organisms:

(1) Nucleic acids that can produce infectious forms of any of the overlap

[1] The importation and interstate movement of VS select agents or toxins listed in paragraphs (c)(1) through (c)(3) of this section may be subject to the permit requirements under part 122 of this subchapter.

[2] However, the importation and interstate movement of these nonviable select agents may be subject to the permit requirements under part 122 of this subchapter.

select agent viruses listed in paragraph (b) of this section.[3]

(2) Recombinant nucleic acids that encode for the functional forms of any overlap toxin listed in paragraph (b) of this section if the nucleic acids:

(i) Can be expressed *in vivo* or *in vitro;* or

(ii) Are in a vector or recombinant host genome and can be expressed *in vivo* or *in vitro.*

(3) Overlap select agents and toxins listed in paragraph (b) of this section that have been genetically modified.

(d) Overlap select agents or toxins that meet any of the following criteria are excluded from the requirements of this part:

(1) Any overlap select agent or toxin that is in its naturally occurring environment, provided that the agent or toxin has not been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source.

(2) Nonviable overlap select agents or nonfunctional overlap toxins.[4]

(3) Overlap toxins under the control of a principal investigator, treating physician or veterinarian, or commercial manufacturer or distributor, if the aggregate amount does not, at any time, exceed the following amounts: 0.5 mg of Botulinum neurotoxins, 100 mg of *Clostridium perfringens* epsilon toxin, 100 mg of Shigatoxin, 5 mg of Staphylococcal enterotoxins, and 1,000 mg of T–2 toxin.

(e) An attenuated strain of an overlap select agent or toxin may be excluded from the requirements of this part based upon a determination that the attenuated strain does not pose a severe threat to public health and safety, to animal health, or to animal products.

(1) To apply for an 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 of the applicant. Exclusions will be published periodically in the notice section of the and will be listed on the Internet at *http://www.aphis.usda.gov/programs/ag_selectagent/index.html.*

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

(3) An individual or entity may make a written request to the Administrator for reconsideration of a decision denying an exclusion application. The written request for reconsideration must state the facts and reasoning upon which the individual or entity relies to show the decision was incorrect. The Administrator will grant or deny the request for reconsideration as promptly as circumstances allow and will state, in writing, the reasons for the decision.

(f) Any overlap select agent or toxin seized by a Federal law enforcement agency will be excluded from the requirements of this part during the period between seizure of the agent or toxin and the transfer or destruction of such agent or toxin provided that:

(1) As soon as practicable, the Federal law enforcement agency transfers the seized agent or toxin to an entity eligible to receive such agent or toxin or destroys the agent or toxin by a recognized sterilization or inactivation process.

(2) The Federal law enforcement agency safeguards and secures the seized agent or toxin against theft, loss, or release, and reports any theft, loss, or release of such agent or toxin.

(3) The Federal law enforcement agency reports the seizure of the overlap select agent or toxin to APHIS or CDC.

(i) The seizure of any of the following overlap select agents and toxins must be reported within 24 hours by telephone, facsimile, or e-mail: *Bacillus anthracis, Botulinum neurotoxins, Brucella melitensis, Francisella tularensis,* Hendra virus, Nipah virus, Rift Valley fever virus, and Venezuelan equine encephalitis virus. This report must be followed by submission of APHIS/CDC Form 4 within 7 calendar days after seizure of the overlap select agent or toxin.

(ii) For all other overlap select agents or toxins, APHIS/CDC Form 4 must be submitted within 7 calendar days after seizure of the agent or toxin.

(iii) A copy of APHIS/CDC Form 4 must be maintained for 3 years.

(4) The Federal law enforcement agency reports the final disposition of the overlap select agent or toxin by submission of APHIS/CDC Form 4. A copy of the completed form must be maintained for 3 years.

121.5 [illegible]

(a) Diagnostic laboratories and other entities that possess, use, or transfer a VS select agent or toxin that is contained in a specimen presented for diagnosis or verification will be exempt from the requirements of this part for such agent or toxin contained in the specimen, provided that:

(1) Unless directed otherwise by the Administrator, within 7 calendar days after identification, the agent or toxin is transferred in accordance with § 121.16 or destroyed on-site by a recognized sterilization or inactivation process;

(2) The agent or toxin is secured against theft, loss, or release during the period between identification of the agent or toxin and transfer or destruction of such agent or toxin, and any theft, loss, or release of such agent or toxin is reported; and

(3) The identification of the agent or toxin is reported to APHIS or CDC.

(i) The identification of any of the following select agents and toxins must be immediately reported by telephone, facsimile, or e-mail: African horse sickness virus, African swine fever virus, avian influenza virus (highly pathogenic), bovine spongiform encephalopathy agent, classical swine fever virus, foot-and-mouth disease virus, Newcastle disease virus (velogenic), rinderpest virus, and swine vesicular disease virus. This report must be followed by submission of APHIS/CDC Form 4 within 7 calendar days after identification.

(ii) For all other VS select agents or toxins, APHIS/CDC Form 4 must be submitted within 7 calendar days after identification.

(iii) Less stringent reporting may be required during agricultural emergencies or outbreaks, or in endemic areas.

(iv) A copy of APHIS/CDC Form 4 must be maintained for 3 years.

(b) Diagnostic laboratories and other entities that possess, use, or transfer a VS select agent or toxin that is contained in a specimen presented for proficiency testing will be exempt from the requirements of this part for such agent or toxin contained in the specimen, provided that:

(1) Unless directed otherwise by the Administrator, within 90 calendar days of receipt, the agent or toxin is transferred in accordance with § 121.16 or destroyed on-site by a recognized sterilization or inactivation process;

(2) The agent or toxin is secured against theft, loss, or release during the period between identification of the agent or toxin and transfer or destruction of such agent or toxin, and any theft, loss, or release of such agent or toxin is reported; and

(3) The identification of the agent or toxin, and its derivative, is reported to APHIS or CDC. To report the

[3] The importation and interstate movement of overlap select agents or toxins listed in paragraphs (c)(1) through (c)(3) of this section may be subject to the permit requirements under part 122 of this subchapter.

[4] However, the importation and interstate movement of these nonviable overlap select agents may be subject to the permit requirements under part 122 of this subchapter.

identification of a select agent or toxin, APHIS/CDC Form 4 must be submitted

supporting scientific information. A written decision granting or denying the request will be issued.

121.14 [illegible].[10]

(a) An individual or entity required to register under this part must develop and implement a written incident response plan.[11] The incident response plan must be coordinated with any entity-wide plans, kept in the workplace, and available to employees for review.

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

(c) The incident response plan must also contain the following information:

(1) The name and contact information (*e.g.*, home and work) for the individual or entity (*e.g.*, responsible official, alternate responsible official(s), biosafety officer, etc.);

(2) The name and contact information for the building owner and/or manager, where applicable;

(3) The name and contact information for tenant offices, where applicable;

(4) The name and contact information for the physical security official for the building, where applicable;

(5) Personnel roles and lines of authority and communication;

(6) Planning and coordination with local emergency responders;

(7) Procedures to be followed by employees performing rescue or medical duties;

(8) Emergency medical treatment and first aid;

(9) A list of personal protective and emergency equipment, and their locations;

(10) Site security and control;

(11) Procedures for emergency evacuation, including type of evacuation, exit route assignments, safe distances, and places of refuge; and

(12) Decontamination procedures.

(d) The plan must be reviewed annually and revised as necessary. Drills or exercises must be conducted at least annually to test and evaluate the effectiveness of the plan. The plan must be reviewed and revised, as necessary, after any drill or exercise and after any incident.

[illegible]

[illegible]

[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.

[12] For guidance, see the CDC/NIH publication, ''Biosafety in Microbiological and Biomedical Laboratories.'' This document is available on the Internet at *http://www.aphis.usda.gov/programs/ag_selectagent/index.html.*

[13] The requirements of this section do not apply to transfers within a registered entity (*i.e.*, the sender and the recipient are covered by the same certificate of registration).