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DEPARTMENT OF AGRICULTURE

Animal and Plant Health Inspection Service

7 CFR Part 331

9 CFR Part 121

[Docket No. APHIS-2014-0095]

RIN 0579-AE08

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

AGENCY: Animal and Plant Health Inspection Service, USDA.

ACTION: Final rule.

SUMMARY: In accordance with the Agricultural Bioterrorism Protection Act of 2002, we are amending and republishing the list of select agents and toxins that have the potential to pose a severe threat to animal or plant health, or to animal or plant products. The Act requires the biennial review and republication of the list of select agents and toxins and the revision of the list as necessary. This action will amend the regulations in several ways, including the addition of provisions to address the inactivation of select agents, provisions addressing biocontainment and biosafety, and clarification of regulatory language concerning security, training, incident response, and records. These changes will increase the usability of the select agent regulations as well as providing for enhanced program oversight. After carefully considering the technical

input of subject matter experts and recommendations from Federal advisory groups, we have decided not to finalize the proposed changes to the contents of the list of select agents and toxins at this time. In a companion document published in this issue of the Federal Register, the Centers for Disease Control and Prevention has made parallel regulatory changes.

DATES: Effective [Insert date 30 days after date of publication in the Federal Register].

FOR FURTHER INFORMATION CONTACT: Dr. Freeda Isaac, National Director, Agriculture Select Agent Services, APHIS, 4700 River Road Unit 2, Riverdale, MD 20737-1231; (301) 851-3300, Option 3.

SUPPLEMENTARY INFORMATION:

Background

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

for Disease Control and Prevention (CDC), which has the primary responsibility for implementing the provisions of the Bioterrorism Response Act for the Department of Health and Human Services (HHS).

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

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

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

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

On January 19, 2016, we published in the Federal Register (81 FR 2762-2774, Docket No. APHIS-2014-0095) a proposal¹ to amend and republish the list of select agents and toxins that have the potential to pose a severe threat to animal or plant health, or to animal or plant products, and amend the regulations in order to add definitions and clarify language concerning security, training, biosafety, biocontainment, and incident response.

We solicited comments concerning our proposal for 60 days ending March 21, 2016. We received 24 comments by that date. They were from researchers, scientific organizations, industry groups, laboratories, and universities. Eighteen were supportive of the proposed action. The remaining six comments are discussed below by topic.

Removal of Select Agents and Toxins

We proposed to amend the list of PPQ select agents and toxins listed in 7 CFR 331.3 by removing three PPQ select agents and toxins from the list: Peronosclerospora philippinensis (Peronosclerospora sacchari), Sclerophthora rayssiae, and Phoma glycinicola (formerly Pyrenochaeta glycines).

¹ To view the proposed rule and the comments we received, go to <http://www.regulations.gov/#!docketDetail;D=APHIS-2014-0095>.

We also proposed to remove three overlap select agents and toxins from the list set out in 9 CFR 121.4(b): Bacillus anthracis (Pasteur strain), Brucella abortus and Brucella suis.

After carefully considering the technical input of subject matter experts and recommendations from Federal advisory groups, we have decided not to finalize the proposed changes to the list of select agents and toxins at this time.

Definitions

In 7 CFR 331.1 and 9 CFR 121.1, we proposed to add definitions for inactivation and kill curve to clarify terms contained within the proposed inactivation provisions. As detailed later in this final rule, we have removed the requirement for generation of a kill curve. We are therefore not including the definition in the regulations.

One commenter suggested that we specify that a “validated method” was used for inactivation. The commenter said that the addition of the word “validated” would ensure that tested and appropriate methods of inactivation would be utilized.

We are eliminating the definition for inactivation and instead adding a definition of validated inactivation procedure to the regulations. This definition encompasses the prior definition of inactivation as well as providing further detail which we believe will be useful for regulated entities. Validated inactivation procedure is defined as a procedure, whose efficacy is confirmed by data generated from a viability testing protocol, to render a select agent non-viable but allows the select agent to retain characteristics of interest for future use; or to render any nucleic acids that can produce infectious forms of any select agent virus non-infectious for future use. While the commenter suggested we use the term “method,” we have decided to use the term “procedure” in response to comments received on the CDC docket.

The same commenter suggested that we add definitions of validated sterility test and safety margin as these terms were both proposed for use in the biocontainment and biosafety sections and could prove confusing or be subject to misinterpretation.

Given that we are adding a definition of validated inactivation procedure as described previously, we are not adding a definition of validated sterility test. We are not adding a definition of safety margin since that term will not be in the regulations.

While we did not receive any further comments regarding definitions, in response to comments received by CDC and in the interests of maintaining parity between the APHIS and CDC regulations, we are adding a definition for viability testing protocol. That term, which is now used in §§ 331.3, 121.3, and 121.4, is defined as, “a protocol to confirm the validated inactivation procedure by demonstrating the inability of a select agent to replicate.”

Exclusions and Inactivation

We proposed to amend 7 CFR 331.3(d)(2), 9 CFR 121.3(d)(2), and 9 CFR 121.4(d)(2), which exclude nonviable select agents or nonfunctional toxins from the requirements of the regulations, in order to clarify our policy that an entity must use a validated procedure to render a select agent nonviable or regulated nucleic acids non-infectious for future use. This means that the method must be scientifically sound and that it will produce consistent results each time it is used.

One commenter stated that we need to consistently address toxins throughout the regulations and suggested adding language specifying that required methods would also render a select toxin as nonfunctional.

We did not include language concerning toxins because, unlike select agents, toxins do not replicate. An inactivation failure with a toxin therefore represents a lower level of risk and thus does not justify the potential additional recordkeeping and reporting burden for registered entities at this time. We may revisit this issue in the future.

We proposed that inactivation include the use of one of the following: The exact conditions of a commonly accepted method that has been validated as applied (e.g., autoclaving), a published method with adherence to the exact published conditions (i.e., extrapolations or deductions are to be avoided), or in-house methods, only if validation testing includes the specific conditions used and appropriate controls.

The same commenter also suggested that we require that the inactivation process be repeatable.

We agree with the commenter that the inactivation process has to be validated so that the results are repeatable. The definition of validated inactivation procedure states that the procedure must be supported by data generated from viability testing. A process that is not repeatable would never be validated.

We also proposed that the entity develop a site-specific kill curve in order to define the conditions of inactivation for each select agent or regulated nucleic acid. If there are strain-to-strain variations in the resistance of a select agent to the inactivation procedure, then a specific kill curve would have to be developed for each strain that undergoes the inactivation procedure. A new kill curve would have to be created upon any change in procedure or inactivation equipment. In addition, a validated sterility testing protocol would have to be conducted in order to ensure that the inactivation method has rendered a select agent nonviable or regulated nucleic acids non-infectious.

Several commenters raised objections regarding development and use of the kill curve. We have considered these comments and determined that the kill curve and safety margin requirements are not applicable to all inactivation procedures and should therefore not be included in the regulations. We are instead requiring that registered entities develop a validated inactivation procedure by establishing parameters for quantities of starting material and measures of uncertainty for repeated successful inactivation. This is a broad performance standard that will allow for flexibility given the variety of select agents and toxins under regulation.² In addition, for the sake of clarity and efficiency, we have removed the requirements specific to extracts of select agents, instead including them within the overall performance standard for select agents and toxins as a whole.

One commenter said that, without more specific direction, the subjectivity of individual inspectors would be the principal factor in determining acceptable inactivation verification.

We will not review or approve inactivation protocols. We believe this activity should be approved at the entity, which will allow for researchers to continue to develop new inactivation procedures. However, inspectors will verify that the entity has developed a validated inactivation procedure and will review viability testing results during the entity's inspection.

Another commenter asked that we provide minimum requirements for the sterility testing protocol and specify whether or not this must be site-specific or if validated methods of sterility testing given in published journal articles may be followed.

² Additional guidance regarding this performance standard has been developed and is available on the Internet at www.selectagents.gov.

We recognize that the limits of detection of the viability testing procedures and expected variation from run to run, even when following an inactivation procedure precisely precludes demonstrating full sterility of an inactivated sample. These sources of error must be considered when the entity establishes performance parameters for inactivation procedures. While complete sterility is not a feasible goal for material that is intended for further use, we expect that the risk of live agent in materials that are removed from containment and are thus no longer subject to select agent requirements will be as low as realistically possible from both a safety and security perspective. We will be addressing the need for onsite validation of both inactivation protocols and viability testing in guidance.

The same commenter cited the guidance document entitled “Non-viable Select Agents and Nonfunctional Select Toxins and Rendering Samples Free of Select Agents and Toxins,”³ which states that, “this guidance does not apply to inactivation for waste disposal.” The commenter urged us to clearly and accurately describe what is intended regarding verification of non-viability in the regulations, stating that they had received comments from some inspectors indicating confusion between inactivation validation requirements for moving materials to a lower containment level and inactivation validation requirements for waste disposal.

We have modified the reporting requirements to require the responsible official to investigate any viability of material that was subjected to a validated inactivation protocol to determine the reason of the inactivation failure. If the responsible official is unable to determine the reason for this failure, he or she must report the inactivation failure to CDC or APHIS. Our intention is to require registered entities to create an environment where inactivation failures are

³ You may view this guidance document on the Internet at <http://www.selectagents.gov/guidance-nonviable.html>.

investigated to determine the root source of the errors instead of re-subjecting the material to an inactivation method that may be flawed or faulty. The revised language only requires reporting of inactivation failures to CDC or APHIS when the responsible official cannot determine the reason for the inactivation failure. We are also clarifying that these provisions apply only to those select agents inactivated for future use as non-select agents and not those intended for waste disposal.

Two commenters asked about the minimum percentage of samples required to be tested to constitute a “representative sample.” Another commenter suggested that inactivated lots be stored with documentation that demonstrates that the lot has met the established standard, but added that it is impractical to conduct validated sterility testing on every sample that is inactivated. The commenter claimed that implementing such a requirement would waste specimens where limited volumes are available, be costly in terms of technical time and resources, and is scientifically unjustified.

Successful implementation of the required validated inactivation procedure and the subsequent data derived from viability testing using that procedure will determine the extent of sampling required. We have removed the sterility testing requirement to allow entities flexibility in establishing and utilizing individualized, validated inactivation procedures.

We also proposed to require that an entity conduct an annual review of their site-specific standard operating procedures to ensure that select agents or regulated nucleic acids that can produce infectious forms of any select agent virus are inactivated by a safety margin and revise as necessary.

Two commenters questioned our use of the term “safety margin.” The commenters requested that we remove or define the term, as its meaning is unclear. The commenters further stated that the need for including a safety margin is unclear and appears superfluous if the intent of the requirement is to define the conditions that achieve conditions that render 100 percent of the select agent non-viable or noninfectious.

We are not defining “safety margin” as the proposed regulatory text using this term will not be incorporated into the final rule.

Finally, we proposed that written records be kept for any select agent that has been rendered nonviable or regulated nucleic acids that have been rendered non-infectious.

Two commenters asked for clarification of the actions constituting review, including description of any documentation that will be expected to demonstrate compliance with the requirement. The commenters wanted to know if it was our expectation that the kill curve and sterility testing be repeated and verified annually, or if this is a review of data and written procedures.

In response, we have modified the language regarding review of site-specific standard operating inactivation procedures to clarify that the entity should review these procedures to determine if they are being adhered to by staff. The annual review requirement does not necessarily involve revalidating inactivation procedures. This review may simply take the form of an evaluation of the site-specific standard operating inactivation procedures to ensure the inactivation conditions used and upper agent limits found in validation data are consistent and that the entity staff are following the site-specific standard operating inactivation procedures. At times an entity may need to revalidate inactivation procedures during the annual review. For

example, review may be needed if the entity finds that staff are not adhering to standard operating procedures or if the entity wants to deviate from the established, validated inactivation procedure.

While we did not receive any further comments on this issue, in response to comments received by CDC and in the interests of maintaining parity between the APHIS and CDC regulations, we have made the following changes:

- Establishing that surrogate strains that are known to possess properties equivalent to select agents may be used to validate the required inactivation procedures under certain conditions;
- Replacing the term “extract” with “material containing a select agent” to clarify that the inactivation requirements apply to such materials as serums or liquid cultures from which select agents are typically removed via filtration without first undergoing inactivation. This is intended to more accurately describe an element of a two-step process: An inactivation step to destroy the select agent and a second step intended to remove any remaining, viable select agent; and
- Clarification of when an entity may submit a waiver request to the Administrator as well as the procedure for such determinations.

Finally, in 7 CFR 331.3(d)(2), 9 CFR 121.3(d)(2), and 9 CFR 121.4(d)(2), we are replacing the term “nonfunctional toxin” with “nontoxic toxin.” We have determined that the term “nonfunctional” is overbroad and has caused confusion. Our intent was to exclude toxins that can no longer exert their toxic effect and cause disease. For example, Botulinum neurotoxin has three functional domains: Binding domain, translocation domain, and catalytic domain. Each functional domain may be solely manipulated such that the toxin is no longer toxic and

does not cause disease even though the other two domains may remain functional. Note that the example provided is for a CDC toxin due to the fact that APHIS does not currently regulate any select toxins.

Exemptions for Select Agents and Toxins

The provisions of 7 CFR 331.5, 9 CFR 121.5, and 9 CFR 121.6 concern conditions under which entities may be exempted from the requirements of the regulations. We proposed to add language to paragraph (a) in 7 CFR 331.5, 9 CFR 121.5, and 9 CFR 121.6 that specifies that entities may be required to report identification of agents or toxins to other appropriate authorities when required by Federal, State, or local law. Specifically, we proposed to add provisions that state that we do not regulate material containing select agents or toxins when it is in a patient care setting and is not being collected or otherwise tested or retained, nor do we regulate waste generated during delivery of patient care. However, once delivery of patient care for the select agent or toxin infection has concluded, waste would become subject to the requirements of the regulations. If an entity cannot meet these requirements, then the material may be transferred to another entity according to the select agent regulations or destroyed using an approved method. The decision to retain, transfer, or destroy any specimens must be made within 7 calendar days of the conclusion of patient care.

One commenter disagreed with adding such a provision to 9 CFR 121.5. The commenter said that VS should have authority to regulate waste and carcasses from animals (i.e., veterinary patients) naturally infected with select agents to ensure that infection does not spread to other livestock or poultry. The commenter asked that we alter the wording of the proposed section in order to specify that the requirement refers to human patients only.

The provisions the commenter refers to relate to the care of human patients only. However, it should be noted that any waste or carcasses from animals infected with a select agent, provided the select agent or toxin has not been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source, are already listed as excluded in §§ 121.3(d)(1) and 121.4(d)(1) of the regulations.

While we did not receive any further comments on this issue, in response to comments received by CDC and in the interests of maintaining parity between the APHIS and CDC regulations, we are amending the text to clarify the following:

- That patient care refers to actions by health care professionals;
- To clarify that destruction and transfer requirements apply solely to waste generated in the course of patient care and not specimens or samples taken from the patient; and
- That specimens taken from a patient are not subject to the regulations during the period in which they are directly associated with the diagnosis, but all specimens taken and kept more than 7 days after the conclusion of patient care are subject to the regulations.

Security, Biocontainment/Biosafety, and Incident Response Plans

The regulations require registered entities to develop and implement a number of plans in order to ensure the safety and security of the select agents they handle. These are:

- A security plan, as described by the regulations in 7 CFR 331.11 and 9 CFR 121.11, that provides for measures sufficient to safeguard the select agent or toxin against unauthorized access, theft, loss, or release;

- A biocontainment plan, in the case of PPQ select agents, or a biosafety plan, in the case of VS and overlap select agents, as described in the regulations in 7 CFR 331.12 and 9 CFR 121.12, that provides for measures sufficient to contain the select agent or toxin (e.g., physical structure and features of the entity, and operational and procedural safeguards); and
- An incident response plan, as described in the regulations in 7 CFR 331.14 and 9 CFR 121.14, that provides for measures that the registered entity will implement in the event of 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.

All of these plans require annual review and revision as necessary. Drills or exercises must also be conducted at least annually to test and evaluate the effectiveness of the plans. The plans must be reviewed and revised, as necessary, after any drill or exercise and after any incident. We proposed to require that these drills or exercises be documented to include how the drill or exercise tested and evaluated the plan, any problems identified, any corrective action taken, and the names of the individuals who participated in the drill or exercise. This will provide a more thorough accounting of required activities as well as increasing the efficacy of the plans via testing and entity-directed improvements. We proposed to add these requirements to 7 CFR 331.11(h), 331.12(e), 331.14(f), 9 CFR 121.11(h), 121.12(e), and 121.14(f).

One commenter stated that the requirement to record the names of the individuals who participated in a given drill or exercise should be limited to registered entity personnel and not include first responders or others who participate. The commenter suggested that a list of the participating external agencies (e.g., emergency management, emergency medical services, fire department, etc.) could be included.

We agree with the commenter's suggestion and have updated the regulations in order to clarify that only the names of individuals at the registered entity are required to be listed. The entity may choose to list the names of external agencies (e.g., fire department, police department, etc.) that participated in the drill or exercise.

Comments on more specific proposed changes to these plans may be found below.

Biocontainment/Biosafety Plan

Paragraph (a) of 7 CFR 331.12 and 9 CFR 121.12 requires that the biocontainment or biosafety plan contain sufficient information and documentation to describe the biosafety and containment procedures for each select agent or toxin that the registered entity will possess. The plan must also include a description of the biosafety and containment procedures for any animals (including arthropods) or plants intentionally or accidentally exposed to or infected with a select agent. We proposed to additionally require that laboratory-specific biocontainment and/or biosafety manuals must be accessible to individuals working in those laboratories. This change will help to foster an enhanced culture of responsibility by ensuring that appropriate biocontainment and/or biosafety resources are available to all staff with access to select agents and toxins within a select agent laboratory.

One commenter suggested that the specific practice of making manuals accessible is already employed by registered entities. The commenter therefore questioned the need for a separate requirement.

We agree with the commenter and have removed the requirement.

Two commenters urged that, “a description of the biosafety and containment procedures for any animals (including arthropods) or plants intentionally or accidentally exposed to or infected with a select agent” should clearly refer not only to animals within the laboratory but also wildlife, domestic, and stray animals outside of the buildings if they are potentially exposed via accidental release. The commenter added that there should be a system in place to detect such incidents if they occur.

The term “any animals” includes both laboratory animals as well as the wild, domestic, and stray animals described by the commenters. We will, however, add specific clarification to the guidance documents associated with the biocontainment and biosafety plans.

One commenter requested clarification regarding the term “laboratory.” The commenter wanted to know whether the term refers to a single room, a building, or to a group of rooms (e.g., laboratory, animal room, and necropsy) used by a principal investigator for a research project. The commenter also requested clarification regarding the phrase, “must be available to each individual working in the laboratory,” asking if this would require creation of a specific biocontainment or biosafety manual for each room.

We have clarified the language to state that “biosafety and containment procedures specific to use of the select agent or toxin by the principal investigator must be available to each individual involved with that project.” This more appropriately ties the creation and distribution of biocontainment and biosafety manuals to specific projects, select agents, and people.

We also proposed to add specific provisions to the biocontainment and biosafety plans that would require completion of a written risk assessment for each procedure.

Two commenters stated that these requirements are unnecessary and would prove excessively burdensome to researchers and the responsible official and should be removed. The commenters said that the new requirements regarding validation of inactivation procedures would serve the same security function. The commenters added that APHIS already has opportunity to review and require amendment of an entity's biocontainment or biosafety plan as a condition of registration or as a result of inspection.

We agree with the commenter that this level of detail would prove unnecessarily burdensome. We have instead added language to 7 CFR 331.12(a)(1) and 9 CFR 331.12(a)(1) to explicitly require that the biocontainment and biosafety plans include a description of the hazardous characteristics of each agent or toxin listed on the entity's registration and the biosecurity or biosafety risk associated with laboratory procedures related to the select agent or toxin.

One commenter asked that we define "risk assessment," given that it is a very broad term and therefore open to interpretation. This commenter and another requested that we provide basic templates for these new required sections and indicate where registered entities and entities seeking registration may find these templates.

We have revised and condensed the proposed language as a result of this and other comments. It no longer includes the term "risk assessment."

Training

We proposed to amend the regulations in 7 CFR 331.15 and 9 CFR 121.15, which concern provision of mandatory training for staff and visitors who work in or visit areas where select agents or toxins are handled or stored. We proposed to require that all individuals who have received approval to have access to select agents and toxins must undergo training regardless of whether they have access to those select agents or toxins. The training would have to be completed within a year of that individual's approval or prior to entry into an area where select agents and toxins are used or stored, whichever occurs first.

Two commenters objected to the proposed addition, stating that we should include a description of the level of training necessary for personnel in varying positions with highly disparate job duties and responsibilities. The commenters requested that we clarify that required training will be conducted at a level appropriate to the registered person's role and level of access to select agents.

We agree with the commenters' point and have altered the required training language to clearly delineate the types of training required for individuals with varying access levels.

One commenter asked that we clearly specify the requirements for both initial and annual training. The commenter also asked that we consider making training a prerequisite for access to select agents and toxins.

While we made no changes to our regulatory language based on this comment, the document entitled, "Guidance for Meeting the Training Requirements of the Select Agent Regulations"⁴ will be updated to provide further detail and assistance regarding the content of

⁴ You may view this document on the Internet at <http://www.selectagents.gov/guidance-training.html>.

initial and annual training. The regulations in 7 CFR 331.15(a)(1) and 9 CFR 121.15(a)(1) already require that each approved individual receive information and training on biosecurity/biosafety, security (including security awareness), and incident response before that individual has access to any select agents and toxins.

Records

The regulations in 7 CFR 331.17 and 9 CFR 121.17 concern required recordkeeping procedures for regulated entities as those records relate to select agents and toxins. Paragraph (a)(3)(x) requires that registered entities record the destruction of any toxins by specifically noting the quantity of toxin destroyed, the date of such action, and by whom. However, there is not an equivalent requirement regarding the destruction of select agents. We proposed to add this requirement in order to ensure consistency with the toxin provisions and ensure proper tracking of select agents from acquisition to destruction.

While we did not receive any comments on this issue, in response to comments received by CDC and in the interests of maintaining parity between the APHIS and CDC regulations, we are amending the text to stipulate that registered entities must maintain a record of the select agent used, purpose of use, and, when applicable, final disposition (including destruction) for each select agent held in long-term storage.

We also proposed to state that any records created that contain information related to an entity's registration or its select agents and toxins must be provided promptly upon request. We proposed to specify that such records may include, but are not limited to, biocontainment certifications, laboratory notebooks, institutional biosafety and/or animal use committee minutes and approved protocols, and records associated with occupational health and suitability programs.

One commenter expressed concern regarding the requirement to keep laboratory notebooks for inspection purposes. The commenter stated that items may include proprietary intellectual property and requested clarification regarding the information needed from the notebooks. The commenter asked that we amend the regulatory language in order to protect intellectual property interests and specify if any information would be required from laboratory notebooks apart from that collected for inventory purposes.

We agree with the commenter and we have clarified that only information related to the requirements of the regulations must be produced upon request. Such information may be found in biocontainment certifications, laboratory notebooks, institutional biosecurity/biosafety and/or animal use committee minutes and approved protocols, and records associated with occupational health and suitability programs. Accordingly, we will only be reviewing relevant portions of any laboratory notebooks or documents and only if they contain information related to any requirements of the regulations.

To ensure the accuracy of handwritten records, we also proposed to specify that such records must be legible.

Another commenter suggested that we require that records be written in ink and not pencil and should be signed and dated when appropriate.

We acknowledge this suggestion as good practice. However, in the interests of not being overly prescriptive, we are leaving the interpretation of “legible” up to individual registered entities.

Records for Select Agents in Long-Term Storage

Paragraph (a)(1) in both 7 CFR 331.17 and 9 CFR 121.17 requires entities to maintain an accurate, current inventory for each select agent (including viral genetic elements, recombinant and/or synthetic nucleic acids, and organisms containing recombinant and/or synthetic nucleic acids) held in long-term storage. We continue to receive comments critical of that portion of the regulations. Criticism is typically focused on the belief that a container-based inventory requirement is not a useful mechanism to track inventory of biological agents, since small amounts could be stolen without detection and used to grow larger quantities.

However, the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 obliges APHIS and CDC to include a requirement for “the prompt notification of the Secretary, and appropriate Federal, State, and local law enforcement agencies, of the theft or loss of listed agents and toxins” in the regulations. We therefore solicited comment regarding what regulatory requirement or requirements should be implemented such that a registered entity could quickly determine whether a select agent had been lost or stolen from long-term storage without that registered entity first having an accurate, current inventory for each select agent held in long-term storage. Additionally, we solicited ideas concerning ways in which the current regulations could be amended to address the possibility of theft of a select agent from a container held in long-term storage.

One commenter stated that, while they understand the need for such inventory and notification requirements, an enormous amount of time and effort is spent during inspections validating that inventories are accurate. The commenter said that this has resulted in the loss of valuable virus isolates due to unintentional thawing, failure of ultralow temperature freezers due to repeated opening and the resulting loss of ultralow temperature, and inefficient use of

employee time. The commenter said that measuring the volumes of stored vials of bacteria and viruses in the manner that toxins or other non-replicative select agents are inventoried is illogical. The commenter acknowledged that it is important to indicate the nature of the pathogens stored and the numbers of vials in freezer stocks, but even the most fastidious recordkeeping could not demonstrate that vials of replicative organisms had not been accessed. The commenter stated that current select agent practices allow for these stocks to be maintained in tamper-evident stocks (e.g., security ties on freezer boxes) so that vials are not individually removed, thawed, and measured. The commenter concluded that requiring the use of tools of this nature in the case of replicative organisms is a logical step that would not eliminate the need to inventory, but which also would not degrade samples and allow for detection of samples that may have disappeared.

We appreciate this comment and will continue to consider how the recognition of theft and loss might be addressed through alternative approaches.

Miscellaneous Changes

We are also adding a definition of principal investigator to the regulations in 7 CFR 331.1 and 9 CFR 121.1 as it is used but not defined in the APHIS regulations. The addition also serves to maintain parity with the CDC regulations. Our definition is identical to that used by CDC.

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

Executive Order 12866 and Regulatory Flexibility Act

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

In accordance with 5 U.S.C. 604, we have performed a final regulatory flexibility analysis, which is summarized below, regarding the economic effects of this rule on small entities. Copies of the full analysis are available on the Regulations.gov Web site (see footnote 1 in this document for a link to Regulations.gov) or by contacting the person listed under FOR FURTHER INFORMATION CONTACT.

Sections 201 and 212(a)(2) of the Act require a biennial review and republication of the select agent and toxin list, with revisions as appropriate in accordance with this law. This final rule will implement the recommendations of the fourth biennial review of select agent regulations and has finalized changes that will increase their usability as well as provide for enhanced program oversight. These amendments include new provisions regarding the inactivation of select agents, specific biosafety and toxin requirements and clarification of regulatory language concerning security, training, and records. The final rule will require that entities develop a validated inactivation procedure by establishing parameters for quantities of starting material and measures of uncertainty for repeated successful inactivation. This is a broad performance standard that will allow for flexibility given the variety of select agents and toxins under regulation to define conditions of inactivation for each select agent or regulated infectious nucleic acid and maintain written records of having done so. Costs of complying with this amendment are expected to be modest.

Currently, there are 291 entities registered with APHIS and CDC. Of these entities, there are 240 registered to possess Tier 1 select agents and toxins, including 78 academic, 29 commercial, 80 State government, 37 Federal government, and 16 private (non-profit) institutions, most of which are considered to be small entities. Based on current recordkeeping and reporting requirements, an additional 10 to 20 hours per year may be required for maintaining records associated with select agents or material containing select agents or regulated nucleic acids that can produce infectious forms of any select agent virus that have been subjected to a validated inactivation procedure or a procedure for removal of viable select agents. At an imputed cost of \$33.40 per hour (GS-12, step 2), this additional time requirement per entity will cost between \$334 and \$668 per year, or in total for all registered entities between \$80,000 and \$160,000. Assuming that costs of the rule could be considered to be significant if they exceeded 1 percent of revenue earned by the affected entities, revenues would need to average less than \$33,400 to \$66,800 for this to be the case. While the vast majority of the entities in industries potentially affected by this rule, other than post-secondary institutions, can be considered small, average annual revenues are well above this range.

Due to the reasons summarized here and explained in the analysis accompanying this rule, the Administrator certifies that this action will not have a significant economic impact on a substantial number of small entities.

Executive Order 12988

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

Executive Order 13175

This rule has been reviewed in accordance with the requirements of Executive Order 13175, Consultation and Coordination with Indian Tribal Governments. Executive Order 13175 requires Federal agencies to consult and coordinate with tribes on a government-to-government basis on policies that have tribal implications, including regulations, legislative comments or proposed legislation, and other policy statements or actions that have substantial direct effects on one or more Indian tribes, on the relationship between the Federal Government and Indian tribes or on the distribution of power and responsibilities between the Federal Government and Indian tribes.

The Animal and Plant Health Inspection Service has assessed the impact of this rule on Indian tribes and determined that this rule does not, to our knowledge, have tribal implications that require tribal consultation under E.O. 13175. If a Tribe requests consultation, the Animal and Plant Health Inspection Service will work with the Office of Tribal Relations to ensure meaningful consultation is provided where changes, additions and modifications identified herein are not expressly mandated by Congress.

Paperwork Reduction Act

In accordance with section 3507(d) of the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 et seq.), the reporting, recordkeeping, and third-party disclosure requirements included in this rule are in the process of being reinstated by the Office of Management and Budget under 0579-0213.

E-Government Act Compliance

The Animal and Plant Health Inspection Service is committed to compliance with the E-Government Act to promote the use of the Internet and other information technologies, to provide increased opportunities for citizen access to Government information and services, and for other purposes. For information pertinent to E-Government Act compliance related to this rule, please contact Ms. Kimberly Hardy, APHIS' Information Collection Coordinator, at 301-851-2483.

List of Subjects

7 CFR Part 331

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

9 CFR Part 121

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

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

Title 7—Agriculture

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

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

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

2. Section 331.1 is amended by adding, in alphabetical order, definitions of principal investigator, validated inactivation procedure, and viability testing protocol to read as follows:

§ 331.1 Definitions.

* * * * *

Principal investigator. The one individual who is designated by the entity to direct a project or program and who is responsible to the entity for the scientific and technical direction of that project or program.

* * * * *

Validated inactivation procedure. A procedure, whose efficacy is confirmed by data generated from a viability testing protocol, to render a select agent non-viable but allows the select agent to retain characteristics of interest for future use; or to render any nucleic acids that can produce infectious forms of any select agent virus non-infectious for future use.

* * * * *

Viability testing protocol. A protocol to confirm the validated inactivation procedure by demonstrating the material is free of all viable select agent.

3. Section 331.3 is amended as follows:
 - a. By revising paragraph (d)(2).
 - b. By redesignating paragraph (d)(3) as paragraph (d)(9)
 - c. By adding paragraphs (d)(3) through (8) and (e)(3).

The additions and revision read as follows:

§ 331.3 PPQ select agents and toxins.

* * * * *

(d) * * *

(2) Nonviable select agents or nontoxic toxins.

(3) A select agent or toxin that has been subjected to decontamination or a destruction procedure when intended for waste disposal.

(4) A select agent or regulated nucleic acids that can produce infectious forms of any select agent virus that has been subjected to a validated inactivation procedure that is confirmed through a viability testing protocol. Surrogate strains that are known to possess equivalent properties with respect to inactivation can be used to validate an inactivation procedure; however, if there are known strain-to-strain variations in the resistance of a select agent to an inactivation procedure, then an inactivation procedure validated on a lesser resistant strain must also be validated on the more resistant strains.

(5) Material containing a select agent that is subjected to a procedure that removes all viable select agent cells, spores, or virus particles if the material is subjected to a viability testing protocol to ensure that the removal method has rendered the material free of all viable select agent.

(6) A select agent or regulated nucleic acids that can produce infectious forms of any select agent virus not subjected to a validated inactivation procedure or material containing a select agent not subjected to a procedure that removes all viable select agent cells, spores, or virus particles if the material is determined by the Administrator to be effectively inactivated or effectively removed. To apply for a determination an individual or entity must submit a written request and supporting scientific information to APHIS. A written decision granting or denying the request will be issued.

(7) A PPQ select toxin identified in an original food sample or clinical sample.

(8) Waste generated during the delivery of patient care by health care professionals from a patient diagnosed with an illness or condition associated with a select agent, where that waste is decontaminated or transferred for destruction by complying with State and Federal regulations within 7 calendar days of the conclusion of patient care.

* * * * *

(e) * * *

(3) An individual or entity may make a written request to the Administrator for reconsideration of a decision denying an application for the exclusion of an attenuated strain of a select agent or a select toxin modified to be less potent or toxic. 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.

* * * * *

4. Section 331.5 is amended as follows:

- a. By revising paragraph (a)(1).
- b. In paragraph (a)(2), by removing “; and” and adding a period in its place.
- c. By revising paragraph (a)(3).

The revisions read as follows:

§ 331.5 Exemptions.

(a) * * *

(1) Unless directed otherwise by the Administrator, within 7 calendar days after identification of the select agent or toxin, the select agent or toxin is transferred in accordance with § 331.16 or destroyed on-site by a recognized sterilization or inactivation process.

* * * * *

(3) The identification of the agent or toxin is reported to APHIS or CDC, the specimen provider, and to other appropriate authorities when required by Federal, State, or local law by telephone, facsimile, or e-mail. This report must be followed by submission of APHIS/CDC Form 4 to APHIS or CDC within 7 calendar days after identification.

* * * * *

5. Section 331.7 is amended as follows:

a. By redesignating paragraphs (b) through (k) as paragraphs (c) through (l), respectively.

b. By adding a new paragraph (b).

The addition reads as follows:

§ 331.7 Registration and related security risk assessments.

* * * * *

(b) As a condition of registration, each entity is required to be in compliance with the requirements of this part for select agents and toxins listed on the registration regardless of whether the entity is in actual possession of the select agent or toxin. With regard to toxins, the entity registered for possession, use, or transfer of a toxin must be in compliance with the requirements of this part regardless of the amount of toxins currently in its possession.

* * * * *

6. Section 331.9 is amended as follows:

a. By removing the semicolons at the ends of paragraphs (a)(1) through (4) and “; and” at the end of paragraph (a)(5) and adding periods in their place.

b. In paragraph (a)(6), by removing the word “laboratory” and adding the words “registered space” in its place and by adding the words “and the corrections documented” at the end of the second sentence after the words “must be corrected”.

c. By adding paragraphs (a)(7), (8), and (9).

The additions read as follows:

§ 331.9 Responsible official.

(a) * * *

(7) Ensure that individuals are provided the contact information for the USDA Office of Inspector General Hotline and the HHS Office of Inspector General Hotline so that they may anonymously report any biosafety/biocontainment or security concerns related to select agents and toxins.

(8) Investigate to determine the reason for any failure of a validated inactivation procedure or any failure to remove viable select agent from material. If the responsible official is unable to determine the cause of a deviation from a validated inactivation procedure or a

viable select agent removal method; or receives any report of any inactivation failure after the movement of material to another location, the responsible official must report immediately by telephone or e-mail the inactivation or viable agent removal method failure to APHIS or CDC.

(9) Review, and revise as necessary, each of the entity's validated inactivation procedures or viable select agent removal methods. The review must be conducted annually or after any change in principal investigator, change in the validated inactivation procedure or viable select agent removal method, or failure of the validated inactivation procedure or viable select agent removal method. The review must be documented and training must be conducted if there are any changes to the validated inactivation procedure, viable select agent removal method, or viability testing protocol.

* * * * *

7. In § 331.10, paragraph (e) is amended by adding a sentence at the end of the paragraph to read as follows:

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

* * * * *

(e) * * * A responsible official must immediately notify the responsible official of the visiting entity if the person's access to select agents or toxins has been terminated.

* * * * *

8. Section 331.11 is amended as follows:

a. In paragraph (c)(5), by adding the word "keycards," after the word "keys," and by removing the word "numbers" and adding the word "permissions" in its place.

b. In paragraph (d)(7)(iv), by removing the word "and".

c. By adding paragraph (d)(7)(vi).

d. By adding a sentence at the end of paragraph (h).

The additions read as follows:

§ 331.11 Security.

* * * * *

(d) * * *

(7) * * *

(vi) Any loss of computer, hard drive or other data storage device containing information that can be used to gain access to select agents or toxins; and

* * * * *

(h) * * * Drills or exercises must be documented to include how the drill or exercise tested and evaluated the plan, any problems that were identified and corrective action(s) taken, and the names of registered entity personnel participants.

9. Section 331.12 is amended as follows:

- a. By revising paragraph (a).
- b. By adding a sentence at the end of paragraph (e).

The addition and revision read as follows:

§ 331.12 Biocontainment.

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

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

infected with a select agent. The current biocontainment plan must be submitted for initial registration, renewal of registration, or when requested. The biocontainment plan must include the following provisions:

(1) The hazardous characteristics of each agent or toxin listed on the entity's registration and the biocontainment risk associated with laboratory procedures related to the select agent or toxin;

(2) Safeguards in place with associated work practices to protect entity personnel, the public, and the environment from exposure to the select agent or toxin including, but not limited to: Personal protective equipment and other safety equipment; containment equipment including, but not limited to, biological safety cabinets, animal caging systems, and centrifuge safety containers; and engineering controls and other facility safeguards;

(3) Written procedures for each validated method used for disinfection, decontamination, or destruction, as appropriate, of all contaminated or presumptively contaminated materials including, but not limited to: Cultures and other materials related to the propagation of select agents or toxins, items related to the analysis of select agents and toxins, personal protective equipment, arthropod containment systems, extracted plant and/or arthropod tissues, laboratory surfaces and equipment, and effluent material; and

(4) Procedures for the handling of select agents and toxins in the same spaces with non-select agents and toxins to prevent unintentional contamination.

* * * * *

(e) * * * Drills or exercises must be documented to include how the drill or exercise tested and evaluated the plan, any problems that were identified and corrective action(s) taken, and the names of registered entity personnel participants.

10. Section 331.14 is amended as follows:

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

b. By adding a sentence at the end of paragraph (f).

The additions read as follows:

§ 331.14 Incident response.⁵

(a) * * * The current incident response plan must be submitted for initial registration, renewal of registration, or when requested.

* * * * *

(f) * * * Drills or exercises must be documented to include how the drill or exercise tested and evaluated the plan, any problems that were identified and corrective action(s) taken, and the names of registered entity personnel participants.

11. Section 331.15 is amended as follows:

a. By revising paragraph (a).

b. By adding paragraph (e).

The addition and revision read as follows:

§ 331.15 Training.

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

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

(1) Each individual with access approval from the Administrator or HHS Secretary. The training must address the particular needs of the individual, the work they will do, and the risks posed by the select agents or toxins. The training must be accomplished prior to the individual's entry into an area where a select agent is handled or stored, or within 12 months of the date the individual was approved by the Administrator or the HHS Secretary for access, whichever is earlier.

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

* * * * *

(e) The responsible official must ensure and document that individuals are provided the contact information of the USDA Office of Inspector General Hotline and the HHS Office of Inspector General Hotline so that they may anonymously report any safety or security concerns related to select agents and toxins.

12. In § 331.16, paragraph (b) introductory text is revised to read as follows:

§ 331.16 Transfers.

* * * * *

(b) A transfer may be authorized if:

* * * * *

13. Section 331.17 is amended as follows:

a. In paragraph (a)(1)(iii), by adding the words “or other storage container” after the word “freezer”.

b. By revising paragraph (a)(1)(v).

c. In paragraph (a)(3)(v), by adding the words “or other storage container” after the word “freezer”.

d. By removing the word “and” at the end of paragraph (a)(6) and removing the period at the end of paragraph (a)(7) and adding “; and” in its place.

e. By adding paragraph (a)(8).

f. By revising paragraphs (b) and (c).

The addition and revisions read as follows:

§ 331.17 Records.

(a) * * *

(1) * * *

(v) The select agent used, purpose of use, and, when applicable, final disposition;

* * * * *

(8) For select agents or material containing select agents or regulated nucleic acids that can produce infectious forms of any select agent virus that have been subjected to a validated inactivation procedure or a procedure for removal of viable select agent:

(i) A written description of the validated inactivation procedure or viable select agent removal method used, including validation data;

(ii) A written description of the viability testing protocol used;

(iii) A written description of the investigation conducted by the entity responsible official involving an inactivation or viable select agent removal failure and the corrective actions taken;

(iv) The name of each individual performing the validated inactivation or viable select agent removal method;

(v) The date(s) the validated inactivation or viable select agent removal method was completed;

(vi) The location where the validated inactivation or viable select agent removal method was performed; and

(vii) A certificate, signed by the principal investigator, that includes the date of inactivation or viable select agent removal, the validated inactivation or viable select agent removal method used, and the name of the principal investigator. A copy of the certificate must accompany any transfer of inactivated or select agent removed material.

(b) The individual or entity must implement a system to ensure that all records and databases created under this part are accurate and legible, have controlled access, and that their authenticity may be verified.

(c) The individual or entity must promptly produce upon request any information that is related to the requirements of this part but is not otherwise contained in a record required to be kept by this section. The location of such information may include, but is not limited to,

biocontainment certifications, laboratory notebooks, institutional biosafety and/or animal use committee minutes and approved protocols, and records associated with occupational health and suitability programs. All records created under this part must be maintained for 3 years.

Title 9—Animals and Animal Products

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

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

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

15. Section 121.1 is amended by adding, in alphabetical order, definitions of principal investigator, validated inactivation procedure, and viability testing protocol to read as follows:

§ 121.1 Definitions.

* * * * *

Principal investigator. The one individual who is designated by the entity to direct a project or program and who is responsible to the entity for the scientific and technical direction of that project or program.

* * * * *

Validated inactivation procedure. A procedure, whose efficacy is confirmed by data generated from a viability testing protocol, to render a select agent non-viable but allows the select agent to retain characteristics of interest for future use; or to render any nucleic acids that can produce infectious forms of any select agent virus non-infectious for future use.

* * * * *

Viability testing protocol. A protocol to confirm the validated inactivation procedure by demonstrating the material is free of all viable select agent.

* * * * *

16. Section 121.3 is amended as follows:

- a. By revising paragraph (d)(2).
- b. By redesignating paragraph (d)(3) as paragraph (d)(4).
- c. By adding a new paragraph (d)(3).
- d. By revising newly redesignated paragraph (d)(4).
- e. By adding paragraphs (d)(5) through (9) and (e)(3).

The additions and revisions read as follows:

§ 121.3 VS select agents and toxins.

* * * * *

(d) * * *

(2) Nonviable VS select agents or nontoxic VS toxins.³

(3) A select agent or toxin that has been subjected to decontamination or a destruction procedure when intended for waste disposal.

(4) A select agent or regulated nucleic acids that can produce infectious forms of any select agent virus that has been subjected to a validated inactivation procedure that is confirmed through a viability testing protocol. Surrogate strains that are known to possess equivalent properties with respect to inactivation can be used to validate an inactivation procedure; however, if there are known strain-to-strain variations in the resistance of a select agent to an inactivation procedure, then an inactivation procedure validated on a lesser resistant strain must also be validated on the more resistant strains.

³ However, the importation and interstate movement of these nonviable select agents may be subject to the permit requirements under part 122 of this subchapter.

(5) Material containing a select agent that is subjected to a procedure that removes all viable select agent cells, spores, or virus particles if the material is subjected to a viability testing protocol to ensure that the removal method has rendered the material free of all viable select agent.

(6) A select agent or regulated nucleic acids that can produce infectious forms of any select agent virus not subjected to a validated inactivation procedure or material containing a select agent not subjected to a procedure that removes all viable select agent cells, spores, or virus particles if the material is determined by the Administrator to be effectively inactivated or effectively removed. To apply for a determination an individual or entity must submit a written request and supporting scientific information to APHIS. A written decision granting or denying the request will be issued.

(7) A VS select toxin identified in an original food sample or clinical sample.

(8) Waste generated during the delivery of patient care by health care professionals from a patient diagnosed with an illness or condition associated with a select agent, where that waste is decontaminated or transferred for destruction by complying with State and Federal regulations within 7 calendar days of the conclusion of patient care.

(9) Any low pathogenic strains of avian influenza virus, avian paramyxovirus serotype-1 (APMV-1) viruses which do not meet the criteria for Newcastle disease virus,⁴ including those identified as pigeon paramyxovirus-12⁵ isolated from a non-poultry species, all subspecies

⁴ An APMV-1 virus isolated from poultry which has an intracerebral pathogenicity index in day-old chicks (*Gallus gallus*) of 0.7 or greater or has an amino acid sequence at the fusion (F) protein cleavage site that is consistent with virulent strains of Newcastle disease virus. A failure to detect a cleavage site that is consistent with virulent strains does not confirm the absence of a virulent virus.

⁵ Pigeon paramyxovirus (PPMV-1) is a species-adapted APMV-1 virus which is endemic in pigeons and doves in the United States and can be identified through monoclonal antibody testing and demonstration of their characteristic amino acid signature at the fusion gene cleavage site.

Mycoplasma capricolum except subspecies capripneumoniae (contagious caprine pleuropneumonia), and all subspecies Mycoplasma mycoides except subspecies mycoides small colony (Mmm SC) (contagious bovine pleuropneumonia), provided that the individual or entity can identify that the agent is within the exclusion category.

(e) * * *

(3) An individual or entity may make a written request to the Administrator for reconsideration of a decision denying an application for the exclusion of an attenuated strain of a select agent or a select toxin modified to be less potent or toxic. 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.

* * * * *

17. Section 121.4 is amended as follows:

- a. In paragraph (c)(1), by redesignating footnote 4 as footnote 6.
- b. In paragraph (c)(2) introductory text, by removing the word “functional” and adding in its place the word “toxic”.
- c. By revising paragraph (d)(2).
- d. By redesignating paragraph (d)(3) as paragraph (d)(9).
- e. By adding paragraphs (d)(3) through (8) and (e)(3).

The additions and revision read as follows:

§ 121.4 Overlap select agents and toxins.

* * * * *

(d) * * *

(2) Nonviable overlap select agents or nontoxic overlap toxins.⁷

(3) A select agent or toxin that has been subjected to decontamination or a destruction procedure when intended for waste disposal.

(4) A select agent or regulated nucleic acids that can produce infectious forms of any select agent virus that has been subjected to a validated inactivation procedure that is confirmed through a viability testing protocol. Surrogate strains that are known to possess equivalent properties with respect to inactivation can be used to validate an inactivation procedure; however, if there are known strain-to-strain variations in the resistance of a select agent to an inactivation procedure, then an inactivation procedure validated on a lesser resistant strain must also be validated on the more resistant strains.

(5) Material containing a select agent that is subjected to a procedure that removes all viable select agent cells, spores, or virus particles if the material is subjected to a viability testing protocol to ensure that the removal method has rendered the material free of all viable select agent.

(6) A select agent or regulated nucleic acids that can produce infectious forms of any select agent virus not subjected to a validated inactivation procedure or material containing a select agent not subjected to a procedure that removes all viable select agent cells, spores, or virus particles if the material is determined by the Administrator or HHS Secretary to be

⁷ 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.

effectively inactivated or effectively removed. To apply for a determination an individual or entity must submit a written request and supporting scientific information to APHIS or CDC. A written decision granting or denying the request will be issued.

(7) An overlap select toxin identified in an original food sample or clinical sample.

(8) Waste generated during the delivery of patient care by health care professionals from a patient diagnosed with an illness or condition associated with a select agent, where that waste is decontaminated or transferred for destruction by complying with State and Federal regulations within 7 calendar days of the conclusion of patient care.

* * * * *

(e) * * *

(3) An individual or entity may make a written request to the Administrator or HHS Secretary for reconsideration of a decision denying an application for the exclusion of an attenuated strain of a select agent or a select toxin modified to be less potent or toxic. 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 or HHS Secretary will grant or deny the request for reconsideration as promptly as circumstances allow and will state, in writing, the reasons for the decision.

* * * * *

18. In § 121.5, paragraph (a) is revised as follows:

§ 121.5 Exemptions for VS select agents and toxins.

(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 of the select agent or toxin, the select 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;

(3) Unless otherwise directed by the Administrator, the clinical or diagnostic specimens collected from a patient infected with a select agent are transferred in accordance with § 121.16 or destroyed on-site by a recognized sterilization or inactivation process within 7 calendar days after delivery of patient care by health care professionals has concluded; and

(4) The identification of the agent or toxin is reported to APHIS or CDC, the specimen provider, and to other appropriate authorities when required by Federal, State, or local law by telephone, facsimile, or e-mail. This report must be followed by submission of APHIS/CDC Form 4 to APHIS or CDC within 7 calendar days after identification.

* * * * *

19. Section 121.6 is amended as follows:

a. By revising paragraph (a)(1).

- b. In paragraph (a)(2), by removing the word “and” at the end of the paragraph.
- c. By redesignating paragraph (a)(3) as paragraph (a)(4).
- d. By adding new paragraph (a)(3).
- e. By revising newly redesignated paragraph (a)(4).

The addition and revisions read as follows:

§ 121.6 Exemptions for overlap select agents and toxins.

(a) * * *

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

* * * * *

(3) Unless otherwise directed by the Administrator or HHS Secretary, the clinical or diagnostic specimens collected from a patient infected with a select agent are transferred in accordance with § 121.16 or destroyed on-site by a recognized sterilization or inactivation process within 7 calendar days after delivery of patient care by health care professionals has concluded; and

(4) The identification of the agent or toxin is reported to APHIS or CDC, the specimen provider, and to other appropriate authorities when required by Federal, State, or local law by telephone, facsimile, or e-mail. This report must be followed by submission of APHIS/CDC Form 4 to APHIS or CDC within 7 calendar days after identification.

* * * * *

20. Section 121.7 is amended as follows:

- a. By redesignating paragraphs (b) through (k) as paragraphs (c) through (l), respectively.
- b. By adding a new paragraph (b).
- c. In newly redesignated paragraph (d)(3) introductory text, by redesignating footnote 6 as footnote 8.
- d. In newly redesignated paragraph (i)(1), by redesignating footnote 7 as footnote 9.

The addition reads as follows:

§ 121.7 Registration and related security risk assessments.

* * * * *

(b) As a condition of registration, each entity is required to be in compliance with the requirements of this part for select agents and toxins listed on the registration regardless of whether the entity is in actual possession of the select agent or toxin. With regard to toxins, the entity registered for possession, use, or transfer of a toxin must be in compliance with the requirements of this part regardless of the amount of toxins currently in its possession.

* * * * *

§ 121.8 [Amended]

21. In § 121.8, footnote 8 is redesignated as footnote 10.

22. Section 121.9 is amended as follows:

a. By removing the semicolons at the ends of paragraphs (a)(1) through (4) and “; and” at the end of paragraph (a)(5) an adding periods in their place.

b. In paragraph (a)(6), by removing the word “laboratory” and adding the words “registered space” in its place and by adding the words “and the corrections documented” at the end of the second sentence after the words “must be corrected”.

c. By adding paragraphs (a)(7), (8), and (9).

The additions read as follows:

§ 121.9 Responsible official.

(a) * * *

(7) Ensure that individuals are provided the contact information for the USDA Office of Inspector General Hotline and the HHS Office of Inspector General Hotline so that they may anonymously report any biosafety/biocontainment or security concerns related to select agents and toxins.

(8) Investigate to determine the reason for any failure of a validated inactivation procedure or any failure to remove viable select agent from material. If the responsible official is unable to determine the cause of a deviation from a validated inactivation procedure or a viable select agent removal method; or receives any report of any inactivation failure after the movement of material to another location, the responsible official must report immediately by telephone or e-mail the inactivation or viable agent removal method failure to APHIS or CDC.

(9) Review, and revise as necessary, each of the entity's validated inactivation procedures or viable select agent removal methods. The review must be conducted annually or after any change in principal investigator, change in the validated inactivation procedure or viable select agent removal method, or failure of the validated inactivation procedure or viable select agent removal method. The review must be documented and training must be conducted if there are any changes to the validated inactivation procedure, viable select agent removal method, or viability testing protocol.

* * * * *

23. In § 121.10, paragraph (e) is amended by adding a sentence at the end of the paragraph to read as follows:

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

* * * * *

(e) * * * A responsible official must immediately notify the responsible official of the visited entity if the person's access to select agents and toxins has been terminated.

* * * * *

24. Section 121.11 is amended as follows:

a. In paragraph (c)(5), by adding the word "keycards," after the word "keys," and by removing the word "numbers" and adding the word "permissions" in its place.

b. In paragraph (d)(7)(iv), by removing the word "and".

c. By adding paragraph (d)(7)(vi).

d. By adding a sentence at the end of paragraph (h).

The additions read as follows:

§ 121.11 Security.

* * * * *

(d) * * *

(7) * * *

(vi) Any loss of computer, hard drive or other data storage device containing information that could be used to gain access to select agents or toxins; and

* * * * *

(h) * * * Drills or exercises must be documented to include how the drill or exercise tested and evaluated the plan, any problems that were identified and corrective action(s) taken, and the names of registered entity personnel participants.

25. Section 121.12 is amended as follows:

a. By revising paragraph (a).

b. By removing paragraph (c)(2).

c. By redesignating paragraph (c)(3) as paragraph (c)(2), and in newly redesignated paragraph (c)(2), removing the words “NIH Guidelines for Research Involving Recombinant DNA Molecules” and adding in their place the words “NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules”.

d. By adding a sentence at the end of paragraph (e).

The addition and revision read as follows:

§ 121.12 Biosafety.

(a) An individual or entity required to register under this part must develop and implement a written biosafety plan that is commensurate with the risk of the select agent or toxin, given its intended use.¹¹ The biosafety plan must contain sufficient information and documentation to describe the biosafety and containment procedures for the select agent or toxin, including any animals (including arthropods) or plants intentionally or accidentally exposed to or infected with a select agent. The current biosafety plan must be submitted for initial registration, renewal of registration, or when requested. The biosafety plan must include the following provisions:

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

(1) The hazardous characteristics of each agent or toxin listed on the entity’s registration and the biosafety risk associated with laboratory procedures related to the select agent or toxin;

(2) Safeguards in place with associated work practices to protect entity personnel, the public, and the environment from exposure to the select agent or toxin including, but not limited to: Personal protective equipment and other safety equipment; containment equipment including, but not limited to, biological safety cabinets, animal caging systems, and centrifuge safety containers; and engineering controls and other facility safeguards;

(3) Written procedures for each validated method used for disinfection, decontamination, or destruction, as appropriate, of all contaminated or presumptively contaminated materials including, but not limited to: Cultures and other materials related to the propagation of select agents or toxins, items related to the analysis of select agents and toxins, personal protective equipment, animal caging systems and bedding (if applicable), animal carcasses or extracted tissues and fluids (if applicable), laboratory surfaces and equipment, and effluent material; and

(4) Procedures for the handling of select agents and toxins in the same spaces with non-select agents and toxins to prevent unintentional contamination.

* * * * *

(e) * * * Drills or exercises must be documented to include how the drill or exercise tested and evaluated the plan, any problems that were identified and corrective action(s) taken, and the names of registered entity personnel participants.

26. Section 121.14 is amended as follows:

a. In the section heading, by redesignating footnote 10 as footnote 12.

b. In paragraph (a), by redesignating footnote 11 as footnote 13, and by adding a sentence at the end of the paragraph.

c. In paragraph (f), by adding a sentence at the end of the paragraph.

The additions read as follows:

§ 121.14 Incident response.¹²

(a) * * * The current incident response plan must be submitted for initial registration, renewal of registration, or when requested.

* * * * *

(f) * * * Drills or exercises must be documented to include how the drill or exercise tested and evaluated the plan, any problems that were identified and corrective action(s) taken, and the names of registered entity personnel participants.

27. Section 121.15 is amended as follows:

a. By revising paragraph (a).

e. By adding paragraph (e).

The addition and revision read as follows:

§ 121.15 Training.

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

(1) Each individual with access approval from the Administrator or HHS Secretary. The training must address the particular needs of the individual, the work they will do, and the risks posed by the select agents or toxins. The training must be accomplished prior to the individual's

¹² Nothing in this section is meant to supersede or preempt incident response requirements imposed by other statutes or regulations.

entry into an area where a select agent is handled or stored, or within 12 months of the date the individual was approved by the Administrator or the HHS Secretary for access, whichever is earlier.

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

* * * * *

(e) The responsible official must ensure and document that individuals are provided the contact information of the USDA Office of Inspector General Hotline and the HHS Office of Inspector General Hotline so that they may anonymously report any safety or security concerns related to select agents and toxins.

28. Section § 121.16 is amended as follows:

- a. In paragraph (a), by redesignating footnote 12 as footnote 14.
- b. By revising paragraph (b) introductory text.
- c. By adding paragraph (l).

The addition and revision read as follows:

§ 121.16 Transfers.

* * * * *

(b) A transfer may be authorized if:

* * * * *

(l) Transfer the amounts only after the transferor uses due diligence and documents that the recipient has a legitimate need (e.g., prophylactic, protective, bona fide research, or other peaceful purpose) to handle or use such toxins. Information to be documented includes, but is not limited, to the recipient information, toxin and amount transferred, and declaration that the recipient has legitimate purpose to store and use such toxins.

29. Section 121.17 is amended as follows:

a. In paragraph (a)(1)(iii), by adding the words “or other storage container” after the word “freezer”.

b. By revising paragraph (a)(1)(v).

c. In paragraph (a)(3)(v), by adding the words “or other storage container” after the word “freezer”.

d. By removing the word “and” at the end of paragraph (a)(6) and removing the period at the end of paragraph (a)(7) and adding the word “; and” in its place.

e. By adding paragraph (a)(8).

f. By revising paragraphs (b) and (c).

The addition and revisions read as follows:

§ 121.17 Records.

(a) * * *

(1) * * *

(v) The select agent used, purpose of use, and, when applicable, final disposition;

* * * * *

(8) For select agents or material containing select agents or regulated nucleic acids that can produce infectious forms of any select agent virus that have been subjected to a validated inactivation procedure or a procedure for removal of viable select agent:

(i) A written description of the validated inactivation procedure or viable select agent removal method used, including validation data;

(ii) A written description of the viability testing protocol used;

(iii) A written description of the investigation conducted by the entity responsible official involving an inactivation or viable select agent removal failure and the corrective actions taken;

(iv) The name of each individual performing the validated inactivation or viable select agent removal method;

(v) The date(s) the validated inactivation or viable select agent removal method was completed;

(vi) The location where the validated inactivation or viable select agent removal method was performed; and

(vii) A certificate, signed by the principal investigator, that includes the date of inactivation or viable select agent removal, the validated inactivation or viable select agent removal method used, and the name of the principal investigator. A copy of the certificate must accompany any transfer of inactivated or select agent removed material.

(b) The individual or entity must implement a system to ensure that all records and databases created under this part are accurate and legible, have controlled access, and that their authenticity may be verified.

(c) The individual or entity must promptly produce upon request any information that is related to the requirements of this part but is not otherwise contained in a record required to be kept by this section. The location of such information may include, but is not limited to, biocontainment certifications, laboratory notebooks, institutional biosafety and/or animal use committee minutes and approved protocols, and records associated with occupational health and suitability programs. All records created under this part must be maintained for 3 years.

Done in Washington, DC, this 10th day of January 2017.

Elvis S. Cordova,

Acting Under Secretary for Marketing and Regulatory Programs.
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