specified in 2 CFR 200.334 and the requirements of this part;

* * * * *

■ 5. Amend § 172.7 by revising paragraph (a)(1)(iv)(F), the first sentence of paragraph (a)(1)(v)(E), paragraph (b)(1)(i), and the first sentence of paragraph (b)(5)(i) to read as follows:

§ 172.7 Procurement methods and procedures.

(a) * * *

(1) * * *

(iv) * * *

(F) The contracting agency shall retain supporting documentation of the solicitation, proposal, evaluation, and selection of the consultant in accordance with this section and the provisions of 2 CFR 200.334.

(v) * * *

(E) The contracting agency shall retain documentation of negotiation activities and resources used in the analysis of costs to establish elements of the contract in accordance with the provisions of 2 CFR 200.334. * * *

* * * * *

(b) * * *

(1) * * *

(i) STAs and their subrecipients shall comply with procurement requirements established in State and local laws, regulations, policies, and procedures that are not addressed by or are not in conflict with applicable Federal laws and regulations, as specified in 2 CFR part 1201.

* * * * *

(5) * * *

(i) When FAHP funds participate in a consultant services contract, the contracting agency shall receive approval from FHWA, or the STA, as appropriate, before utilizing a consultant to act in a management support role for the contracting agency; unless an alternate approval procedure has been approved. * * *

* * * * *

■ 6. Amend § 172.9 by revising paragraph (a)(3)(iv)(B)(*1*), paragraph (c)(1)(iv), and paragraph (d)(1)(vii) to read as follows:

§ 172.9 Contracts and administration.

(a) * * *

(3) * * *

(iv) * * *

(B) * * *

(*1*) Through an additional qualifications-based selection procedure, which may include, but does not require, a formal RFP in accordance with § 172.7(a)(1)(ii); or

* * * * *

(c) * * *

(1) * * *

(iv) Access by the STA, subrecipient, FHWA, the U.S. Department of Transportation's Inspector General, the Comptroller General of the United States, or any of their duly authorized representatives to any books, documents, papers, and records of the consultant which are directly pertinent to that specific contract for the purpose of making audit, examination, excerpts, and transcriptions;

* * * * *

(d) * * *

(1) * * *

(vii) Documenting contract monitoring activities and maintaining supporting contract records, as specified in 2 CFR 200.334.

* * * * *

■ 7. Amend § 172.11 by revising paragraph (b)(1)(iii) introductory text, the second and third sentences of paragraph (c)(2) introductory text, the second sentence of paragraph (c)(3)(i), and the second and third sentences of paragraph (d) to read as follows:

§ 172.11 Allowable costs and oversight.

* * * * *

(b) * * *

(1) * * *

(iii) When the indirect cost rate has not been established by a cognizant agency in accordance with paragraph (b)(1)(ii) of this section, the STA shall perform an evaluation of a consultant's or subconsultant's indirect cost rate prior to acceptance and application of the rate to contracts administered by the STA or its subrecipients. The evaluation performed by STAs to establish or accept an indirect cost rate shall provide assurance of compliance with the Federal cost principles and may consist of one or more of the following:

* * * * *

(c) * * *

(2) * * * An STA may employ a risk-based oversight process to provide reasonable assurance of consultant compliance with Federal cost principles on FAHP funded contracts administered by the STA or its subrecipients. If employed, this risk-based oversight process shall be incorporated into STA written policies and procedures, as specified in § 172.5(c). * * *

* * * * *

(3) * * *

(i) * * * The certification requirement shall apply to all indirect cost rate proposals submitted by consultants and subconsultants for acceptance by an STA. * * *

* * * * *

(d) * * * FHWA, STAs, and subrecipients of FAHP funds may share audit information in complying with the STA's or subrecipient's acceptance of a consultant's indirect cost rates pursuant to 23 U.S.C. 112 and this part provided that the consultant is given notice of each use and transfer. Audit information shall not be provided to other consultants or any other government agency not sharing the cost data, or to any firm or government agency for purposes other than complying with the STA's or subrecipient's acceptance of a consultant's indirect cost rates pursuant to 23 U.S.C. 112 and this part without the written permission of the affected consultants. * * *

[FR Doc. 2024–01705 Filed 1–29–24; 8:45 am]

BILLING CODE 4910–22–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

[Docket No. CDC–2020–0024]

42 CFR Part 73

RIN 0920–AA71

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

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

ACTION: Notice of proposed rulemaking.

SUMMARY: In accordance with the Public Health Service Act, the Department of Health and Human Services (HHS) Centers for Disease Control and Prevention (CDC) reviewed the HHS list of select agents and toxins with the potential to pose a severe threat to public health and safety. HHS/CDC proposes to amend the list by removing three biological agents, raising one toxin's exclusion amounts, renaming a virus, designating a current agent as a Tier 1 agent, and removing the designation of Tier 1 status from one agent. HHS/CDC also proposes to clarify language and add requirements as discussed below.

DATES: Submit written or electronic comments by April 1, 2024.

ADDRESSES: You may submit comments, identified by Docket No. CDC–2020–0024 or Regulation Identifier Number (RIN) 0920–AA71, by any of the following methods:

- *Federal eRulemaking Portal: https://www.regulations.gov.* Follow the instructions for submitting comments.
- *Mail:* Division of Regulatory Science and Compliance, Centers for Disease Control and Prevention, 1600 Clifton Road NE, Mailstop H21–4,

Atlanta, Georgia 30329, ATTN: RIN 0920–AA71.

Instructions: All submissions received must include the agency name and RIN for this rulemaking. All relevant comments received will be posted without change to *http://www.regulations.gov,* including any personal information provided. Do not send comments by email; CDC does not accept public comment by email.

Docket Access: For access to the docket to read background documents or comments received, or to download an electronic version of the notice of proposed rulemaking, go to *http://www.regulations.gov.*

FOR FURTHER INFORMATION CONTACT: Samuel S. Edwin Ph.D., Director, Division of Regulatory Science and Compliance, Centers for Disease Control and Prevention, 1600 Clifton Road NE, Mailstop H21–7, Atlanta, Georgia 30329. Telephone: (404) 718–2000.

SUPPLEMENTARY INFORMATION: The Notice of Proposed Rulemaking (NPRM) is organized as follows:

I. Public Participation

Interested persons or organizations are invited to participate by submitting written views, recommendations, and data. Comments are welcomed on any topic related to this notice.

In addition, HHS/CDC invites comments specifically as to whether there are additional biological agents or toxins that should be added or removed from the HHS list of select agents and toxins based on the following criteria outlined under 42 U.S.C. 262a(a)(1)(B):

(1) ''The effect on human health of exposure to the agent or toxin''

(2) ''The degree of contagiousness of the agent or toxin and the methods by which the agent or toxin is transferred to humans''

(3) ''The availability and effectiveness of pharmacotherapies to treat or immunizations to prevent any illness resulting from infection by the agent or exposure to the toxin''

(4) ''Any other criteria including the needs of children and other vulnerable populations'' and any other criteria that the commenter believes should be considered.

Comments received, including attachments and other supporting materials, are part of the public record and subject to public disclosure. Commenters should not include any information in their comments or supporting materials that they consider confidential or inappropriate for public disclosure. HHS/CDC will carefully consider all comments submitted in preparation of a final rule. Do not send comments by email. CDC does not accept public comment by email.

II. Background

A. Legal Authority

Under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (Bioterrorism Response Act), the HHS Secretary must establish by regulation, a list of biological agents and toxins that have the potential to pose a severe threat to public health and safety (42 U.S.C. 262a(a)(1)). In determining whether to include a biological agent or toxin on the list, the Bioterrorism Response Act requires that the HHS Secretary consider the following criteria: the effect on human health of exposure to an agent or toxin; the degree of contagiousness of the agent and the methods by which the agent or toxin is transferred to humans; the availability and effectiveness of pharmacotherapies and immunizations to treat and prevent illnesses resulting from an agent or toxin; and any other criteria, including the needs of children and other vulnerable populations that the HHS Secretary deems relevant (42 U.S.C. 262a(a)(1)(B)).

Under 42 U.S.C. 262a(a)(2), the HHS Secretary must review and republish the list of HHS select agents and toxins at least biennially. For this review, HHS/CDC evaluated as discussed below each agent and toxin based on: the degree of pathogenicity (ability of an organism to cause disease); dissemination efficacy; aerosol stability; matrix stability; ease of production; ability to genetically manipulate or alter; severity of illness; case fatality rate; long-term health effects; rate of transmission; available treatment; status of host immunity (*e.g.* whether an individual has already been exposed to the agent and generated an immune response); vulnerability of special populations; decontamination and restoration (the extent remediation efforts are needed due to agent persistence in the environment and population); and the burden or impact on the health care system.

As noted above, the list of HHS select agents and toxins is divided into two sections. The biological agents and toxins listed in 42 CFR 73.3 (HHS select agents and toxins) have the potential to pose a severe threat to human health and safety and are regulated only by HHS. The biological agents listed in 73.4 (overlap select agents and toxins) have not only the potential to pose a severe threat to human health and safety, but have also been determined by the USDA, pursuant to USDA's authority under the Agriculture Bioterrorism Protection Act of 2002 (7 U.S.C. 8401), to have the potential to pose a severe threat to animals and animal products. Accordingly, these biological agents are jointly regulated by HHS and USDA as ''overlap'' select agents. The Bioterrorism Response Act defines the term ''overlap agents and toxins'' to mean biological agents and toxins that are listed pursuant to 42 U.S.C. 262a(a)(1) and listed pursuant to 7 U.S.C. 8401(a)(1). *See* 42 U.S.C. 262a(l) and 7 U.S.C. 8401(l). If HHS/CDC removes any overlap select agents from its list, these agents might still be regulated as USDA select agents dependent on the outcome of the USDA biennial review. The Federal Select Agent Program (FSAP) is the collaboration of the CDC, Division of Regulatory Science and Compliance (previously known as the Division of Select Agents and Toxins) and the USDA Animal and Plant Health Inspection Service (APHIS), Division of Agricultural Select Agents and Toxins to administer the select agent regulations and coordinate federal oversight of select agents and toxins in

a manner to minimize the administrative burden on the regulated community.

B. 2020 ANPRM

On March 17, 2020, we published an advance notice of proposed rulemaking (ANPRM) (85 FR 15087) in which we stated that we were requesting comments on whether to retain or remove three species of *Brucella (B. abortus, B. melitensis,* and *B. suis*), *Rickettsia prowazekii, Coxiella burnetii, Bacillus anthracis* (Pasteur strain), Botulinum neurotoxin producing species of *Clostridium,* and Venezuelan Equine Encephalitis Virus (VEEV) 1AB and 1C. We received 335 comments from the ANPRM. Regarding the request for comment on whether to retain or remove *R. prowazekii, C. burnetii, B. anthracis* (Pasteur strain), Botulinum neurotoxin producing species of *Clostridium,* and VEEV from the select agent and toxins list, HHS/CDC received 27 comments from individuals, animal health groups, regulated communities and public health associations that had mixed opinions on removing and retaining the agents. Of the 16 commenters who supported delisting, the majority of comments supported the delisting of *C. burnetii* and *C. botulinum.* Six commenters believed that *C. burnetii* should be delisted to allow for effective research can be conducted towards the development of improved vaccination for livestock, diagnostics, and other livestock management options and one commenter argued many people may have already been exposed, approximately 60% of exposures remain asymptomatic, and a significant portion of the population may already have immunity. Besides the five comments that cited information found in the ANPRM as a basis for removal, one commenter added that the disease botulism is caused by intoxication with protein toxins, botulinum neurotoxins, and not by intoxication with *C. botulinum.* Another commenter indicated that spores of botulinum neurotoxin species of *Clostridium,* used to conduct food challenge studies should be excluded from the requirements of the regulations. There was only one comment each in support of delisting *R. prowazekii,* VEEV, and *B. anthracis* (Pasteur strain) that supported information found in ANPRM. After carefully reviewing the public comments and considerations for determining whether to include an agent or toxin on the list as articulated in 42 U.S.C. 262a, we are proposing to retain *Rickettsia prowazeckii, Coxiella burnetii,* VEEV, and *B. anthracis* (Pasteur strain) from the select agents and toxins list. The additional changes we are moving forward with in this proposed rule can be found listed below including proposing the removal of *Brucella abortus, Brucella melitensis,* and *Brucella suis.* We also are proposing to raise exclusion amounts for conotoxin, renaming Ebola virus, designating Nipah virus as a Tier 1 select agent, and removing the designation of Tier 1 status from Botulinum neurotoxin producing species of *Clostridium.* We appreciate all comments received from the ANPRM and will consider these comments in future deliberations.

III. Summary of Proposed Changes to 42 CFR Part 73

The following changes to the list of HHS select agents and toxins are proposed based on comments received in response to the advance notice of proposed rulemaking (85 FR 15087) and final rule (82 FR 6278).

HHS/CDC newly proposes to add definitions and provisions to further clarify inactivation of select agents; adding requirements for reporting discoveries of select agents and toxins; provisions regarding effluent decontamination system; and biosafety provisions for facility verification requirements for registered biosafety level 3 and animal biosafety level 3 laboratories.

HHS/CDC also newly proposes to remove *Brucella abortus, Brucella melitensis,* and *Brucella suis* from the select agent list; update the terminology and clarify the specific clade that is a select agent by changing ''Monkeypox virus'' to ''Mpox virus (clade I)''; and to change ''SARS coronavirus (SARS–CoV)'' to ''Severe acute respiratory syndrome coronavirus (SARS–CoV)'' to correct the nomenclature; and to remove the exclusion regarding South American genotype of Eastern Equine Encephalitis virus as this terminology is no longer the correct nomenclature. HHS/CDC is interested in comments regarding these proposed revisions.

In addition, HHS/CDC is proposing to incorporate existing policies previously published and found at *www.selectagents.gov* into regulations and is soliciting public comments on these policies, further discussed below, regarding roles of the Responsible Official and Alternate Responsible Official, chemical inactivation of tissues, conclusion of patient care, annual internal inspections, inactivation certificates, deviation from a validated inactivation procedure or a viable select agent removal method, studies involving naturally infected animals, formalin-fixed paraffin-embedded tissues containing a select agent, validated inactivation procedures, and in-house validation. This is a standard practice for HHS/CDC to utilize policy to first refine its practices before codification. This helps to ensure that regulated entities are able to implement the requirements. In addition, HHS/CDC proposes to correct editorial errors. By codifying these existing policies into regulation, HHS/CDC aims to provide clarity and stability in program requirements, make compliance more straightforward for regulated entities, and ensure enforcement is consistent and predictable across the regulated community.

Specifically, HHS/CDC is seeking comments on whether any of the proposed changes would create an additional burden in implementing the proposed changes.

A. Definitions

HHS/CDC is proposing to add or revise the following eight terms to section 73.1 of the regulations (Definitions) to clarify the use of these terms in the regulations.

The ''loss,'' ''release,'' and ''theft'' definitions are proposed to be added to assist the regulated community on what is to be reported as required under Section 19. The definition of ''discovery'' relates to the proposed new reporting requirement further discussed below. The addition of proposed definitions of ''validated removal procedure'' and ''verification viability testing protocol'' and the revisions of ''validated inactivation procedure'' and ''viability testing protocol'' will provide clarity on inactivation provisions outlined in regulations in Sections 3, 4, 9 and 17. The new terms include:

- Discovery means the finding of a select agent or toxin by an individual or entity that is not aware of the select agent or toxin's existence. Examples include, but are not limited to, the following:

(1) A registered individual or entity finds a select agent or toxin not accounted for in their inventory; or

(2) A non-registered individual or entity finds a select agent or toxin.

- Loss means the inability to account for a select agent or toxin known to be in the individual's or entity's possession.
- Release means any of the following:

(1) an incident resulting in occupational exposure to a select agent or toxin,

(2) an incident resulting in animal/plant exposure to a select agent or toxin,

(3) the failure of equipment used to contain a select agent or toxin such that

it is reasonably anticipated that a select agent or toxin was released,

(4) the failure of or breach in personal protective equipment in the presence of a select agents or toxin, or

(5) the failure of biosafety procedures such that it is reasonably anticipated that a select agent or toxin was outside of containment.

- Theft means the unauthorized taking and removing of a select agent or toxin from the possession of an individual or entity.
- Validated removal procedure means a procedure, whose efficacy has been confirmed by data generated in-house from a viability testing protocol, to remove all viable select agent, or nucleic acids of any select agent virus capable of producing infectious virus.
- Verification viability testing protocol means a protocol, used on samples that have been subjected to a validated inactivation or removal procedure, to confirm the material is free of all viable select agent, or nucleic acids of any select agent virus capable of producing infectious virus.

Existing definitions being revised include:

- Validated inactivation procedure means a procedure, whose efficacy has been confirmed by data generated from an in-house 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 means a protocol used to confirm the efficacy of the inactivation or removal procedure by demonstrating the material is free of all viable select agent, or nucleic acids of any select agent virus capable of producing infectious virus.

B. Removal of Brucella abortus, Brucella melitensis, and Brucella suis

HHS/CDC is proposing removing *B. abortus, B. melitensis,* and *B. suis* from the select agents and toxins list based on a review of considerations outlined under 42 U.S.C. 262a(a)(1)(B). That provision calls for consideration of (1) an agent's effect on human health, (2) degree of contagiousness, (3) the availability and effectiveness of pharmacotherapies and immunizations, and (4) other appropriate criteria as determined by the HHS Secretary. With regard to the effect on human health, *Brucella* infections have a low case fatality rate, with an untreated fatality rate usually ranging from 1–2% of those identified with the infection (Spickler, 2018). Brucellosis typically causes mild clinical symptoms (flu-like illness) (Olsen et al., 2018). With regard to the degree of contagiousness, there is no indication that *Brucella* is transmitted between people by casual contact under ordinary conditions. Humans are typically infected from exposure to animal reservoirs or animal products; transmission to humans from wildlife is a rare event unless an individual directly handles infected animals, such as in butchering meat (Godfroid et al., 2013). With regard to the availability of effective pharmacotherapies, disease caused by these bacteria is treatable with antibiotics (Spickler, 2018).

In the ANPRM, HHS/CDC sought comments on whether *B. abortus, B. melitensis,* and *B. suis* should be removed or retained on the select agents and toxins list, with a substantial majority supporting removal of the agents. HHS/CDC received four comments recommending the retention of *B. abortus, B. melitensis,* and *B. suis* on the list of select agents and toxins. One commenter indicated that if state public health laboratories no longer accept specimens suspected as containing these *Brucella* species for confirmatory testing, then the burden of such confirmatory testing will fall upon the sentinel laboratories of the Laboratory Response Network (LRN). The commenter further argued that all clinical laboratories do not have the engineering controls (*e.g.,* biological safety cabinets) needed to perform these procedures safely and there could be a risk of occupational health and safety concerns if identification activities are not done with appropriate care. Regardless of an agent's status on the select agent list, clinical laboratories will likely continue to be exposed to these agents when conducting diagnostic procedures or working with unknown samples if sufficient biosafety and personal protective measures are not taken. Furthermore, removing an agent from the select agents and toxins list does not preclude state laboratories from providing testing; HHS/CDC does not direct the testing provided by these laboratories. The other commenter agreed with retention because Brucellosis is a very serious human disease and *Brucella* spp. are easily spread in a laboratory environment where laboratory acquired cases are not rare. Another commenter stated that *Brucella* species are known to have a low infectious dose and therefore present an increased risk of infection due to laboratory exposures. In addition, *Brucella* is the top laboratory acquired infection reported by clinical laboratories to public health laboratories. If removed from the select agent list, the commenter stated that it is likely that hospitals will no longer report these exposures, leaving many laboratorians at risk. For these reasons, the commenter recommended that *Brucella* should be stringently regulated and therefore remain as a select agent. While HHS/CDC agrees with the commenters that *Brucella* has a low infectious dose, the case fatality rate and person-to-person transmission for *Brucella* continues to be very low. In addition, the human illnesses are readily recognized and treated.

HHS/CDC received 36 comments that supported removal based on the considerations provided in the ANPRM and stated that the agents should be removed so that important research can be conducted to include vaccine development. Another 286 commenters supported the removal of *B. abortus* to reduce the regulatory burden so that effective research can be conducted towards the development of improved vaccination for livestock, diagnostics, and other livestock management options. Two commenters supported the removal of *B. abortus* and *B. suis* to reduce the regulatory burden to further the development of diagnostic testing, effective vaccines, and further assistance in controlling the agent. Another commenter believes *B. abortus* and *B. suis* to be poor selections for a biological agent. While *B. suis* was one of the first bioweapons developed by the United States in the 1950s, there have been many more insidious and potent pathogens that have been identified in the past 70 years (Olsen et al., 2018). Although *B. abortus* and *B. suis* have zoonotic capabilities, humans are essentially dead-end hosts for brucellosis making it improbable that an infected person can transmit the disease to another person (Olsen et al., 2018). Other disease characteristics of brucellosis, including mild clinical symptoms, the long incubation period, positive response to antibiotic/pharmacotherapy treatment, low risk of human-to-human transmission, and low mortality rate, further decrease the attractiveness of *B. abortus, B. melitensis,* and *B. suis* as bioweapons (Centers for Disease Control and Prevention, 2017; Cross et al., 2019; Shakir, 2021).

In accordance with the criteria and considerations for determining whether to include an agent or toxin on the list as articulated in 42 U.S.C. 262a, HHS/CDC is proposing to remove *B. abortus, B. melitensis,* and *B. suis* from the HHS select agents and toxins list. The minimal effects on human health upon exposure to these agents, the degree of

contagiousness of these agents, the methods by which these agents are transferred to humans, and the availability and effectiveness of pharmacotherapies to treat illness resulting from these agents are key considerations for this proposal. HHS/CDC would be interested in comments on this proposal. Please provide a detailed explanation for your response. Since *B. abortus, B. melitensis,* and *B. suis* are overlap select agents, even if HHS/CDC removes them from its list, these agents might still be regulated as USDA select agents dependent on the outcome of USDA biennial review.

C. Botulinum Neurotoxin Producing Species of Clostridium

Botulism is a serious paralytic disease caused by a neurotoxin produced during the growth of the spore-forming bacterium *Clostridium botulinum* (or rarely, *C. argentinense* (Puig de Centorbi et al., 1997), *C. butyricum,* or *C. baratii*) (Sobel, 2005). In the ANPRM, HHS/CDC requested comment on whether this agent should be removed or retained from the select agents and toxins list because the organism does not normally cause disease. At this time, HHS/CDC is proposing to retain Botulinum neurotoxin producing species of *Clostridium* as an HHS select agent because it produces the highly toxic Botulinum neurotoxin (a select toxin). Given the risk that the agent can produce such a potent toxin, HHS/CDC is proposing to retain this organism as an HHS select agent; however, HHS/CDC is also proposing that because the organism itself does not normally cause disease, it no longer be listed as a Tier 1 agent.

HHS/CDC received mixed reactions on whether to retain or remove the agent. Six comments supported the retention of the agent; however, five supported the removal. Besides the information included in the ANPRM for removal, that the organism does not cause disease, one commenter added that the disease botulism is caused by intoxication with protein toxins, botulinum neurotoxins, and not by intoxication with *C. botulinum.* Therefore, the commenter further explained that human botulism cases are rare and can be managed with antitoxin treatments.

HHS/CDC received one comment that spores of botulinum neurotoxin species of *Clostridium,* used to conduct experimental food challenge studies, should be excluded from the HHS list of select agents because:

- Basic biological safety practices are already sufficient to protect laboratory personnel and the public.
- Inoculated food samples replicate the concentrations of spores that may be naturally found in the foods or soils or sediments.
- Botulinum spores are not infectious to the general public of healthy individuals older than 1 year of age.
- Toxin production for inoculated samples is no greater than that which may occur naturally if a consumer were to mishandle or temperature-abuse low acid foods.

HHS/CDC disagreed that experimental food challenge studies should be excluded from the regulations. Since this work would require possession and manipulation of the select agent Botulinum neurotoxin producing species of *Clostridium,* and is not diagnostic in nature, this work is not exempted from the select agent and toxin regulations. Cells or spores of botulinum neurotoxin producing species of *Clostridia* are introduced into the samples intentionally. Therefore, this work would be regulated by the select agent regulations.

Six commenters did not support the removal of botulinum neurotoxin producing species of *Clostridia.* One commenter recommended that the organism not be considered as Tier 1 select agent. Two commenters argued the bacteria grows and produces toxin relatively easily (Peck, 2009). One commenter further claimed that normally the bacterium exists in the environment as a dormant spore; however, in environments such as in canned foods, deep wounds, or the intestinal tract, the spores germinate into vegetative bacteria. Two commenters stated that with access to these strains, a simplistic grocery-grade broth filled to the maximum volume or neck of a container is enough for the criminals to drive the fermentation process following inoculation of such strains. Another commenter argued that a botulism outbreak, whether natural or deliberate, can quickly overwhelm local health care systems. Commenters further disagreed with the comparison of the organism to *S. aureus* not being regulated, but that its toxins are because the commenters stated that Staphylococcal enterotoxins are not nearly as potent and fatal as botulinum neurotoxin. The other commenter disagreed because in order to produce the purified botulinum neurotoxins that are used in medicine, food safety, and other fields, the commenter argued that it is essential to secure strains or recombinant organisms of neurotoxigenic *Clostridia* for consistent production of high-quality botulinum neurotoxins (*i.e.,* those strains that produce true toxins). Another commenter argued that a terrorist could use the crude toxin cell extracts and not purified toxin for weaponization purposes. Two commenters stated that the removal of the agent status could set a wrong precedence for recombinant strains to express biologically active toxin for easy and bulk production. A commenter also indicated that medical clinicians often use highly purified toxins, but these still need to be made by neurotoxigenic organisms including special strains. As the toxin produced by these species remains regulated, a commenter stated that the agent should be retained since it is not currently standard practice for public health laboratories to quantify toxin levels following identification of *C. botulinum.* If the agent is retained as an HHS select agent, two commenters requested that changes be made to the regulations to: (i) relax the current inventory format of maintaining stocks or working stocks; (ii) relax or remove in-house validation and verification requirements (to test 10% volume or sample size subjected to agent inactivation and/or removal procedures), while implementation of a terminal filtration step to remove the cells or spore forms from the research or analytical samples needs to be continued to ensure the security of the agent; and (iii) include more waiver provisions for *bona fide* research as needed, or on a case by case basis (*e.g.,* food challenge studies, countermeasure development, emergencies, proficiency testing and diagnostics etc.). HHS/CDC disagreed with the commenters that certain provisions should be relaxed. If an individual or entity is registered to possess, use, or transfer a select agent, then the individual or entity is required to meet all the regulatory requirements for the select agent. It should be noted that the current regulations do not contain provisions regarding ''working stocks'' and contain a provision for an individual or entity to obtain a waiver for ''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 HHS Secretary to be effectively inactivated or effectively free of select agent'' (*See* 73.3 (d)(6)).

In accordance with the criteria and considerations for determining whether to include an agent or toxin on the list articulated in 42 U.S.C. 262a, HHS/CDC agreed with the six commenters to retain botulinum neurotoxin producing species of *Clostridia* as an HHS select

agent. HHS/CDC made the determination because the toxin is easily secreted by botulinum neurotoxin producing species of Clostridia which makes it simple to isolate the lethal toxin.

HHS/CDC also agreed and has determined that the botulinum neurotoxin producing species of Clostridia should no longer be identified as a Tier 1 select agent. Tier 1 select agents and toxins pose a severe threat to public health and safety and are considered to present the greatest risk of deliberate misuse with significant potential for mass casualties or devastating effect to the economy, critical infrastructure, or public confidence. Because the organism itself does not meet this definition and does not normally cause widespread disease, HHS/CDC does not believe the organism should be designated as a Tier 1 select agent. HHS/CDC would continue to retain Botulinum neurotoxins as a Tier 1 agent. HHS/CDC would be interested in comments on retaining botulinum neurotoxin producing species of Clostridia as an HHS select agent and not as a Tier 1 select agent. Please provide a detailed explanation for your response.

D. Hantaviruses

In the 2020 ANPRM, HHS/CDC requested public comment on whether Sin Nombre virus (SNV), Andes virus (ANDV), Hantaan virus (HTNV), and Dobrava virus (DOBV) should be considered HHS select agents given the fatality rate and low infectious/lethal doses of these viruses. Based on a review of considerations outlined under 42 U.S.C. 262a(a)(1)(B) and the public comments submitted by subject matter experts, HHS/CDC is not proposing to add these viruses to the select agent list. Specifically, the very limited direct person-to-person transmission of hantaviruses, the difficulty of propagating the organisms in a laboratory setting, and the fact that the infectious dose of hantavirus for humans is higher than the doses provided in ANPRM indicate that these viruses are not appropriate for inclusion on the select agent list.

HHS/CDC received one comment that supported this addition of the viruses as HHS select agents. HHS/CDC received three comments that did not support the addition of these viruses as HHS select agents. The commenters who did not support listing argued that adding these viruses will result in a significant burden on research institutions. For those institutions that already have a select agent program and registered laboratories established, one commenter argued adding new agents may crowd existing laboratory spaces and will likely result in slowed research and development of vaccines and treatments for all agents studied within the space. The commenter further explained that new requirements would take considerable time, delay critical research programs, and require increased funding. Two commenters presented the following reasons to not include these viruses as select agents:

- Current laboratory practices and biosafety regulations do not expose research personnel and the larger community to high risk of hantavirus infection (*e.g.,* direct person-to-person transmission of hantaviruses has not been documented for any hantavirus, except for very limited confirmed events for Andes virus in South America; laboratory-acquired infections have not been documented for these viruses since the adoption of ABSL–3 (HTNV, DOBV) and ABSL–4 (SNV, ANDV) practices; and lack of approved therapeutics and vaccines is not sufficient criteria for select agent inclusion based on other emerging RNA virus classifications (such as West Nile virus, Zika virus, Powassan virus, many non-endemic Influenza A viruses, chikungunya virus).
- The infectious dose of any hantavirus for humans is likely much higher than those presented in the proposal, as evidenced by non-human primate studies and strikingly rare infections despite endemicity in rodent reservoirs and significant ecological overlap between humans and reservoirs.
- These viruses do not pose a national security threat as potential bioweapons due to the notoriously challenging culture conditions of even laboratory-adapted strains and the scarcity of tractable animal models or amplifying hosts.
- This designation of select agent status will significantly disrupt ongoing research operations.

HHS/CDC agreed with two commenters and has decided not to propose adding these Hantaviruses as HHS select agents. As explained above, there has been very limited direct person-to-person transmission. In addition, the infectious dose for humans is likely higher than the doses provided in ANPRM, and it is difficult to propagate in a laboratory setting. HHS/CDC would be interested in comments on adding these Hantaviruses as HHS select agents. Please provide a detailed explanation for your response.

E. Toxin Review: Changes to Exclusion Limits for Short, Paralytic Alpha Conotoxins

HHS/CDC is proposing to increase the exclusion amount for short, paralytic alpha conotoxins from 100mg to 200mg based on assessments of lethal doses of conotoxin compared to other regulated toxins and the amount of the toxin that would be needed if a bad actor sought to weaponize it.

In the 2020 ANPRM (85 FR 15087), HHS/CDC requested comments on whether any toxins should be retained, removed, or if the exclusion amount for each toxin should be increased or decreased. Specifically, HHS/CDC requested comments for short, paralytic alpha conotoxins containing the following amino acid sequence $X_1CCX_2PACGX_3X_4X_5X_6CX_7$. Alpha conotoxins are low, molecular weight toxins that are isolated from the venom bulb of the marine cone snail. These toxins present a public health threat because they are highly toxic, more stable, and can persist for longer periods of time in the environment. Additional toxins requested for public comment include Diacetoxyscirpenol and Staphylococcal enterotoxins.

One commenter agreed with the proposal to remove short, paralytic alpha conotoxins and diacetoxyscirpenol. However, the commenter did not provide any rationale to why these toxins should be removed. The same commenter did not support the removal of Staphylococcal enterotoxins because the toxins, while rarely fatal, cause severe cases of food poisoning. Furthermore, the commenter stated that the toxins have been explored as a potential biological weapon during the cold war. In the 1960's, three different occurrences of laboratory exposure were reported, and the pathogenic dose is extremely low (Pinchuk et al., 2010). The commenter argued that the isolation of Staphylococcal enterotoxins is relatively easy and would make for a nearly untraceable method of bioterrorism as illnesses would most likely be treated as food poisoning due to the mishandling of food. HHS/CDC agreed with the commenter that Staphylococcal enterotoxins should remain as a select toxin because the enterotoxins can cause severe food poisoning and, in rare cases, can be fatal. Since no rationale was provided to remove diacetoxyscirpenol as a select toxin, HHS/CDC has decided it should be retained as an HHS select toxin.

In response to the Notice of Proposed Rulemaking (81 FR 2805), one commenter supported the removal of

short paralytic alpha-conotoxin and one comment opposed the removal of short paralytic alpha-conotoxin. The commenter that opposed removal stated that: (1) the LD_{50} (lethal dose, 50% or median lethal dose, the amount of the substance required (usually per body weight) to kill 50% of the test population) of 20 µg/kg for the short paralytic alpha-conotoxin is not a low toxicity compared to other select agents, and this LD_{50} is actually in line with other marine toxins included on the list, such as Tetrodotoxin and Saxitoxin; (2) the LD_{50} of actual cone snail venom may be lower due to the synergistic effect of multiple conotoxins; and (3) conotoxins can be readily synthesized. The commenter further asserted when using solid phase peptide synthesis, ten grams of toxin is not difficult to produce. HHS/CDC agreed with the commenter and determined that conotoxins (short, paralytic alpha conotoxins containing the following amino acid sequence $X_1CCX_2PACGX_3X_4X_5X_6CX_7$) should be retained as an HHS select toxin because the ability to produce the toxin synthetically is easier now with more modern technology.

While HHS/CDC did not receive any comments regarding whether the exclusion amount for each toxin should be increased or decreased, likely due to insufficient evidence on LD_{50} levels in humans through various routes of intoxication, HHS/CDC is not proposing any changes to the current exclusion limits for the toxins, with the exception of short, paralytic alpha conotoxins. To assess the amount necessary to weaponize a biological toxin, the Department of Homeland Security (DHS) developed toxin parameters and attack scenarios for potential inhalation and ingestion exposures to select toxins. The DHS models determined the impact of the dissemination of varying concentrations of toxin on public health. HHS/CDC believes the amount of each toxin, with the exception of conotoxins, that could be possessed without regulation by a principal investigator, a treating physician or veterinarian, or a commercial manufacturer or distributor was determined on the basis of toxin potency and how much one could safely possess without constituting a potential threat to public safety or raising concerns about use as a weapon that would have a widespread effect. HHS/CDC reviewed the LD_{50} used for the calculations and the ingestion/inhalation scenarios, and the lethal doses of conotoxins are comparable to other regulated toxins with a much higher permissible amount. Therefore, HHS/CDC believes that the exclusion limit can be increased and still not pose a severe threat to public health. In 2017, HHS/CDC inadvertently did not propose an increase in the exclusion limit for short, paralytic alpha conotoxins in the Notice of Proposed Rulemaking (81 FR 2805). Based on the DHS model, HHS/CDC proposes to raise the exclusion limit for conotoxin from 100 mg to 200 mg based on the toxin parameters and attack scenarios for potential inhalation and ingestion exposures to this select toxin. HHS/CDC would be interested in any comments regarding raising the exclusion limit from 100 mg to 200 mg. Please provide a detailed explanation for your response.

F. Renaming Ebola Virus to the Genus Ebolavirus

Recently, the International Committee on Taxonomy of Viruses (ICTV) published a report on the virus family *Filoviridae,* which classified the species of Ebola and Ebola-like viruses that are in the genus *Ebolavirus (*Kuhn et al., 2019). To date, there are six species in the genus *Ebolavirus,* including Ebola virus, Bombali virus, Reston virus, Bundibugyo virus, Sudan virus, and Taï Forest virus. Currently, the HHS/CDC select agent list includes the name Ebola virus to encompass all of the six viruses listed above in the genus *Ebolavirus.* HHS/CDC is seeking public comment on whether Ebola virus, on the HHS/CDC select agent list as a Tier 1 select agent, should be renamed as *Ebolavirus* to agree with the recent taxonomic change by ICTV. Please provide a detailed explanation for your response.

G. Designating Nipah Virus as a Tier 1 Select Agent

Executive Order 13546 ''Optimizing the Security of Biological Select Agents and Toxins in the United States'' directed the HHS Secretary to designate a subset of select agents and toxins that present the greatest risk of deliberate misuse with the most significant potential for mass casualties or devastating effects to the economy, critical infrastructure, or public confidence. This subset of select agents and toxins is identified as Tier 1. In the ANPRM, HHS/CDC sought public comment on whether Nipah virus should be identified as a Tier 1 select agent because the public health threat posed by Nipah virus is similar to that of Marburg and Ebola viruses, in terms of human transmissibility and high case fatality rate, which are both currently Tier 1 agents. It was also noted in the ANPRM that entities that are currently registered to possess Nipah virus are also in possession of other Tier 1 select agents. HHS/CDC received only one comment in support of this proposal. HHS/CDC is proposing Nipah virus should be identified as a Tier 1 select agent because of its:

- Human transmissibility (person-to-person transmission has occurred) (Centers for Disease Control and Prevention, 2014; Gurley et al., 2007; Luby et al., 2012; and Luby et al., 2009).
- High case fatality rate (estimated between 40–100%) (World Health Organization, 2017 and Harcourt et al., 2004).
- Low infectious dose (ranging from 10^1–10^7 plaque forming units depending on route of infection) (DeWit et al., 2014; Geisbert et al., 2010; and Mathieu et al., 2012).
- High severity of illness, including fever, headache, dizziness, vomiting, cough, reduced levels of consciousness, respiratory distress, and in some cases, death (Hossain et al., 2008; and Lo et al., 2008).
- Severe long-term effects, including neurological complications including encephalopathy, cranial nerve palsies, and dystonia (Sejvar et al., 2007 and Lo et al., 2008). These complications and long-term side effects in survivors of Nipah virus infection can also include persistent convulsions and personality changes.

HHS/CDC would be interested in comments on this proposal. Please provide a detailed explanation for your response.

H. Adding a Footnote to the HHS Select Agent List

For viruses, the International Committee on Taxonomy of Viruses (ICTV) is the international group that sets the standards for names of viruses. Commonly accepted names are still used in the virus community, but there is an effort to create a standard nomenclature. The committees are made up of virus specialists around the world (including from HHS/CDC specialists) to standardize nomenclature and work to avoid confusion. HHS/CDC is working to harmonize list of select agent viruses with ICTV to match the international standard. However, we want to ensure that the common names are also reflected (or at least captured) so if a name changes or is modified, then the list of select agent viruses is still accurate. As such, HHS/CDC proposes to add a footnote to the list for HHS select agents indicating that the current nomenclature will be available on the FSAP website (*https://www.selectagents.gov*).

I. Discovery of Select Agents or Toxins

Since the implementation of the select agent and toxin regulations in 2003 (HHS/CDC, 2003), unless a regulatory exemption or exclusion is applied, individuals and entities are required to register with HHS or USDA to possess a select agent or toxin. Possession of regulated material without proper registration is a regulatory violation that could result in civil, criminal, and/or administrative penalties. Since this time, there have been at least 100 instances of reports from entities that ''discovered'' a select agent or toxin in their possession that the individual or entity was neither registered to possess as required. Many of the agents and toxins ''discovered'' were from studies associated with personnel who had left their entity, and the custodianship of samples was not reassigned. Some of the materials were labeled with obsolete pathogen names, while other ''discovered'' material were found in laboratories where their active use had ceased, in some cases, decades prior to the establishment of the select agent and toxin regulations.

HHS/CDC continues to receive reports from entities who find themselves in possession of select agents and toxins that they are not registered to possess. Given these instances, HHS/CDC is proposing to amend section 73.2 of the regulations to clearly state that any individual or entity in possession of a select agent or toxin, for which (1) an exclusion or exemption listed in 42 CFR part 73 does not apply, and (2) that is not included on a certificate of registration issued by the HHS Secretary or USDA Administrator for that individual or entity, must immediately report such possession to either the HHS Secretary or USDA Administrator. This proposal ensures that all discoveries of possession of a select agent or toxin is reported using the proposed new form regardless of if the individual or entity is registered with the program. As such, registered entities that knowingly come into possession of a material prior to amending their registration would report the possession using the proposed form. HHS/CDC would be interested in comments regarding the proposal to ensure the reporting of discovered select agents and toxins including if there is an undue burden being placed on registered entities to report the discovery as well as amending their registration.

To facilitate such reporting, HHS and USDA plan to create, in compliance with the Paperwork Reduction Act, a new APHIS/CDC Form 6 to specify the information that must be submitted regarding the discovery of the select agent or toxin. Establishing a standard form for reporting will enable HHS and USDA to better understand the circumstances and assess regulatory violations related to the possession of ''discovered'' select agents and toxins.

J. Non-Possession of Select Agent or Toxin by a Registered Entity

HHS/CDC is proposing to clarify throughout the regulations that whenever an individual or entity is registered to possess, use or transfer a select agent or toxin, the individual or entity is required to meet all of the regulatory requirements for those select agents and toxins listed on the individual or entity's certificate of registration regardless of whether the select agent or toxin is in the actual possession of the individual or entity and without regard to the amount of toxin possessed. Registration permits an individual or entity to possess select agents and toxins at any time and indicates its readiness to do so.

K. The Electronic Federal Select Agent Program (eFSAP) Information System

HHS/CDC utilizes a highly secure information system, the eFSAP information system, to conduct all select agent program activities. The eFSAP information system is a two-way communication portal, which is accessible by both CDC and APHIS staff and the regulated community. For users at registered entities, benefits of the system include reduced paperwork, increased ease of validating and submitting information, and reduced processing time for requests (as real-time information exchange allows for increased responsiveness). Based on the implementation of the eFSAP information system, HHS/CDC is proposing to update provisions to indicate that reports (*e.g.,* APHIS/CDC Forms 2, 3, and 4) and requests (*e.g.,* amendments to registration) can be submitted via the eFSAP information system (or successor IT system as specified by CDC in guidance). In addition, the electronic documentation in the eFSAP information system serves as official records required by the select agent and toxin regulations, and once submitted in the eFSAP information system, there is no requirement for entities to retain a separate copy.

L. Registration

The certificate of registration is the document issued by the Federal Select Agent Program to an individual or entity that denotes approval to possess, use and/or transfer specified select agents and toxins; the specific activities related to the registered select agents and/or toxins; persons authorized to access the select agents and/or toxins; and the locations (buildings, rooms, suites of rooms, storage facilities, etc.) where select agents and/or toxins are authorized to be present as described in the individual or entity's APHIS/CDC Form 1. The issuance of a certificate of registration may be contingent upon inspection or submission of additional information, such as the security plan, biosafety plan, incident response plan, or any other documents required to be prepared to meet requirements of the select agent and toxin regulations. In addition, the certificate of registration is required to be amended prior to making any changes and must be reauthorized at least every three years from the date it was initially issued or renewed. The individual or entity's certificate of registration must be amended to reflect changes in circumstances relative to the possession and use of select agent and toxins (*e.g.,* replacement of the Responsible Official or other personnel changes, changes in ownership or control of the individual or entity, changes in the locations and activities involving any select agents or toxins, or the addition or removal of select agents or toxins). As such, HHS/CDC is proposing clarification to language to explain that an amendment ''must'' be submitted instead of ''may'' for any changes to the approved certificate of registration. The proposal corrects a discrepancy between language found in (i) that states an amendment may be

submitted versus language found in (i)(1), which states that the Responsible Official must apply for amendment. An entity must submit an amendment prior to making any change. Therefore, the use of ''may'' is not an accurate term. With the use of eFSAP information system instead of the submission of a revised form, HHS/CDC proposes to update language to replace ''additional documents'' to ''additional information'' since information is what is being revised in the system and not documents.

M. Tier 1 Security Enhancements

HHS/CDC is proposing to clarify security enhancements regarding screening visitors for those entities possessing Tier 1 select agents and toxins because HHS/CDC believes the new language clearly specifies the requirements and will aid in compliance. The proposed provision has been revised to read: ''Entities with Tier 1 select agents and toxins must prescribe the following security enhancements: Procedures for screening visitors, their property, and, where appropriate, vehicles at entry and exit points to registered space based on the entity's site-specific risk assessment.'' While HHS/CDC does not have any evidence of non-compliance, HHS/CDC has received feedback from the registered entities requesting clarification on the current provision that reads: ''Procedures for allowing visitors, their property, and vehicles at the entry and exit points to the registered space, or at other designated points of entry to the building, facility, or compound that are based on the entity's site-specific risk assessment.'' HHS/CDC believes the proposed provision will clarify there are multiple checkpoints needed to ensure compliance with the Tier 1 requirement.

N. Biosafety—Facility Verification

HHS/CDC is proposing to require facility verification every 12 months for registered entities that maintain biosafety level 3 and animal biosafety level 3 laboratories. The proposal is to codify the 2014 policy that provided specific provisions for the verifications regarding BSL–3/ABSL–3 facilities to meet the requirements outlined under 42 CFR 73.12(b) ''biosafety and containment procedures must be sufficient to contain the select agent or toxin (*e.g.,* physical structure and features of the entity, and operational and procedural safeguards).'' The verifications also must be documented and validate the facility's containment functions such as inward directional airflow, decontamination systems, and preventative maintenance. Therefore, HHS/CDC is proposing to require the entity to document facility verification and require the entity to verify the facility's containment functions.

HHS/CDC does not believe that the new provisions will create an additional burden to entities that maintain biosafety level 3 and animal biosafety level 3 laboratories since these entities are already performing annual facility verifications. However, if a registered entity has not been performing annual facility verifications for biosafety level 3 and animal biosafety level 3 laboratories, HHS/CDC would be interested in comments concerning the cost and burden of annual facility verifications, especially if the entity is considered a small business.

O. Biosafety—Effluent Decontamination System

Biosafety level 3 and biosafety level 4 facilities are highly sophisticated facilities built to contain biological agents and toxins with the highest potential to threaten agricultural, plant and public health and safety. Any defect, such as a crack or leaky pipe, could have severe consequences. In August 2007, foot-and-mouth disease was discovered at farms in the United Kingdom. The source of the contamination was determined to be long-term damage and leakage of a drainage system used by a high-containment laboratory working with the foot-and-mouth disease virus. Given these risks, HHS/CDC is proposing to amend the security, biosafety, and incident response sections of the select agents and toxins regulations to address risks posed by the effluent decontamination systems used by biosafety level 3 and biosafety level 4 facilities.

If an effluent decontamination system is used by an entity, the entity must include in its plans how it will address security, biosafety, and incident response as it relates to the system. Specifically, the biosafety plan must provide for verification that the liquid waste generated from registered space is sufficiently treated to prevent the release of a select agent or toxin prior to discharge of the waste from the facility. The security plan, for any space not listed on the entity's registration that contains a portion of an effluent decontamination system, must describe procedures to prevent the theft, loss, or unauthorized access to a select agent or toxin. The incident response plan must fully describe the entity's response procedures for the theft, loss, or release of a select agent or toxin; the failure of an effluent decontamination system resulting in a release of a select agent or toxin, and how personnel will access an area potentially containing a select agent or toxin due to the failure of an effluent decontamination system.

P. Restricted Experiments

HHS/CDC proposes to clarify the provision that the receiving entity must amend their certificate of registration and receive approval by CDC or APHIS to possess the products of a restricted experiment. Entities are currently required to obtain approval to conduct restricted experiments and possess the product of a select agent or toxin that results from a restricted experiment. However, the current provisions do not address if the entity comes into possession of a product of a restricted experiment based on the transfer of the agent. This proposal aligns with the registration section where the Responsible Official must apply for an amendment and receive approval prior to any change in the registration, such as the receipt of a product of a restricted experiment. The proposed provisions also ensure receiving entities have the appropriate safeguards in place to receive and possess the product from a transfer.

Q. Training

HHS/CDC is proposing revisions to the training requirements in accordance with the new mandate in the Prepare for and Respond to Existing Viruses, Emerging New Threats, and Pandemics Act (42 U.S.C. 262a(k)(1); Pub. L. 117–328). These revisions have been made in an effort to comply with the statutory amendment that states training requirements for (1) unapproved individuals whose responsibilities routinely place them in close proximity to laboratory facilities and (2) those individuals who perform administrative or oversight functions. Trainings must be completed within 6 months after the final rule is published.

R. Records

HHS/CDC proposes to clarify the records provisions to ensure accurate, current inventory is maintained for each select agent held in long-term storage and all toxins to more clearly specify the requirements and aid in compliance. HHS/CDC is proposing that records contain: (1) the quantity acquired and the name of the individual by whom the select agent or toxin was acquired; (2) the location where it is stored (*e.g.,* building, room number or name, and freezer identification or other storage container); (3) for removal and return of the select agent or toxin from storage, the date the select agent or toxin was

removed and returned, the purpose for using it, the name of the individual who removed and returned it, and when applicable, date of final disposition of the select agent or toxin and by whom; and (4) for intra-entity transfers (sender and the recipient are covered by the same certificate of registration), name of the select agent or toxin, the date of the transfer, the number of items or quantity of the select agent or toxin transferred, the name of the sender, and the name of the recipient. HHS/CDC believes the proposed provision will clarify information needed to ensure the inventory is accurate and complete from the select agents and toxins origination to destruction. Due to prior inquiries received from the regulated community, HHS/CDC is seeking comments on whether the proposed changes are specific enough to ensure proper records are maintained.

S. Codifying Existing Policies

HHS/CDC is proposing to incorporate five existing policies previously published and found at *www.selectagents.gov* into regulations and are soliciting public comments on these policies, further discussed below. By codifying these existing policies into regulation, HHS/CDC aims to provide clarity and stability in program requirements, make compliance more straight-forward for regulated entities, and ensure enforcement is consistent and predictable across the regulated community.

1. Conclusion of Patient Care

HHS/CDC proposes to codify in regulation the current policy that for an individual who has been admitted to a medical facility, the ''conclusion of patient care'' and the point when ''delivery of patient (*i.e.,* human) care by heath care professionals has concluded'' is when an individual is no longer receiving treatment provided by the medical facility or physician. If the patient is seen by the physician or medical facility for follow-up care (*e.g.,* six-month follow-up visit), this would be considered a new delivery of patient care.

The policy also clarified that select agent waste generated during the delivery of patient care applies only to the treatment of humans. Accordingly, specimens or waste associated with that individual (*e.g.,* tissue samples, body fluids, fomites and any other contaminated material likely to transmit an infection to people through the environment if it is unable to be decontaminated) must be destroyed or transferred to a registered individual or entity within seven days after an individual is no longer receiving treatment provided by the medical facility.

2. When Animals Naturally Infected With Select Agents Are Excluded

HHS/CDC proposes to codify in regulation the current policy regarding when animals naturally infected with select agents are excluded from the requirements of the regulations. Sections 73.3(d)(1) and 73.4(d)(1) provide for exclusion of select agents occurring in their natural environment. Mere possession of an animal that is naturally infected with a select agent, either within its natural environment or having been transported to an artificially established environment, meets the criteria of this exclusion. However, the removal of an animal which is naturally infected with a select agent from its natural environment to an artificially established environment for the purpose of

(1) the intentional exposure or introduction of a select agent to a naïve or experimental animal; or

(2) the introduction of a naïve animal to a natural environment where there is an animal that is naturally infected with a select agent for the purpose of the intentional exposure or introduction of a select agent to the naïve or experimental animal, does not meet the exclusion criteria.

If an animal is confirmed to be naturally infected with a select agent, there may be additional transfer and/or transport restrictions based upon other federal or state requirements.

3. Inactivation

HHS/CDC proposes to codify into regulation the current policies regarding inactivation, clarifying and reorganizing the existing provisions regarding select agent inactivation and select agent removal, and clarifying that a certificate must be generated prior to excluding inactivated or select agent-free material.

For chemical inactivation of whole tissue or homogenized tissue, two options are acceptable when choosing appropriate tissue for procedure validation. The first option is to use the tissue that is expected to have the highest concentration of the specific agent to serve as a surrogate for other tissues, including those in other animal models, so long as all standardized conditions (*e.g.,* the agent used, tissue volume, and ratio of tissue to volume of inactivating chemical) are held constant. The second option is to determine the agent concentration in a tissue before performing the inactivation procedure and set this concentration as the maximum agent limit for subsequent inactivation procedures. A safety margin must be incorporated into the final chemical inactivation procedure to ensure the effective inactivation of the agent.

Any select agent or regulated nucleic acid that can produce infectious forms of any select agent virus is excluded if the material is contained in a formalin-fixed paraffin-embedded tissue or fixed to slides (*e.g.,* Gram stain) that have been effectively inactivated by a recognized method for that particular agent or regulated nucleic acid. HHS/CDC also proposes to codify the policy that allows individuals approved by HHS or USDA to access select agents and toxins besides the Responsible Official (*e.g.,* Principal Investigators) to revise the inactivation procedures, if necessary. Principal investigator is defined in the regulations as 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. When a Principal investigator is unavailable (such as out of the office) to review the results of a select agent that has been subjected to a validated inactivation or removal procedure, a temporary designee (appointed by the principal investigator and approved of by the responsible official) may sign the inactivation certificate to allow for work to continue. The temporary designee must be listed on the entity's registration and have the knowledge and expertise to provide scientific and technical direction regarding the validated inactivation procedure or the procedure for removal of viable select agent to which the certificate refers. The appointment of a designee to sign certificates is not for regular substitution of the principal investigator, such as the principal investigator relinquishing this requirement to other individuals in the laboratory due to normal work demands or general unavailability. In addition, HHS/CDC is proposing to codify in regulation the current policies regarding records for inactivated or select agent-free material, to clarify what records are needed for inactivated or select agent-free material (to include allowance of a knowledgeable designee to sign the certificate of inactivation on behalf of a Principal Investigator during his/her absence, a timeframe after inactivation or select agent removal for when certificates must be signed and for how long they must be kept by the entity), and a requirement that certificates accompany all transfers including intra-entity transfers. These proposed provisions clarify the recordkeeping

requirements regarding inactivation procedures and inactivated or select agent-free material. It also allows Principal Investigators to designate individuals to sign on their behalf within seven days after completion of the validated inactivation or validated viable select agent removal, and require a certificate to be maintained for as long as the material is in the possession of the registered individual or entity plus an additional 3 years. The inclusion of the policies into the regulations verifies the material has been inactivated by the subject matter expert and the verification document is available throughout its possession by the entity.

4. Responsible Official and Alternate Responsible Official

HHS/CDC proposes to codify in regulation the current policy that the Responsible Official (RO) cannot be approved as RO at more than one registered individual or entity. We also propose to clarify the policy that a RO cannot be approved to be the sole Alternate Responsible Official (ARO) at another registered individual or entity. This means that the RO can serve as ARO at another registered individual or entity as long as they are not the only ARO at the other individual or entity. In addition, HHS/CDC proposes to codify in regulation that an individual who has been approved as an ARO at one individual or entity can be approved to be an ARO at another registered individual or entity. The 2017 policy statement regarding Approval of a person to be a Responsible Official at only one entity, was necessary and was based on the federal regulations that specify that the RO must ''have a physical (and not merely a telephonic or audio/visual) presence at the registered entity to ensure that the entity is in compliance with the select agent regulations and be able to respond in a timely manner to onsite incidents involving select agents and toxins in accordance with the entity's incident response plan.''

5. Annual Internal Inspections

HHS/CDC proposes to codify in regulation the current policy that an individual or entity's annual internal inspections must address whether:

1. The individual or entity's biosafety/biocontainment plan is being effectively implemented, as outlined in Section 12.

2. The individual or entity's security plan is being effectively implemented, as outlined in Section 11.

3. The individual or entity's incident response plan is implemented to ensure whether the entity is able to respond, as outlined in Section 14.

4. Each individual with access approval from the HHS Secretary or Administrator has received the appropriate training as outlined in Section 15.

The proposal codified the 2019 policy that clarified the language of section 9 (a) based on the HHS' Office of Inspector General's Report, ''Entities Generally Met Federal Select Agent Program Internal Inspection Requirements But CDC Could Do More To Improve Effectiveness'' (OEI–04–15–00431) recommendation ''to clarify to DSAT inspectors and to entities the breadth and depth required for internal inspections, including which of the regulatory sections and subsections of 42 CFR part 73 must be addressed as inspection standards.''

IV. Alternatives Considered

One alternative to the proposed rule considered by HHS was not to propose to codify the current operational policies listed above and to propose the delisting of the select agents. However, we decided to propose codification for the sake of consistency with USDA and transparency with our stakeholders. The proposed changes are currently operationalized, and codification of the policies has been recommended by various governmental entities. Without codification we would not have transparency and consistency throughout agencies which is important when requiring strict adherence to our proposed regulatory policies for select agents; thus, we have rejected the alternative to not codify our operational policies that are closely coordinated between USDA and HHS. Moving forward with codifying the current operational policies listed above and not proposing to delist the select agents through federal notice would not be meeting the regulatory mandate under 42 U.S.C. 262a(a)(2) where the HHS Secretary must review and republish the list of HHS select agents and toxins at least biennially.

V. Required Regulatory Analyses

A. Executive Orders 12866, 13563, and 14094

HHS/CDC has examined the impacts of the NPRM under Executive Order 12866, Regulatory Planning and Review (58 FR 51735, October 4, 1993) and Executive Order 13563, Improving Regulation and Regulatory Review, (76 FR 3821, January 21, 2011). Both Executive Orders direct agencies to evaluate any rule prior to promulgation to determine the regulatory impact in terms of costs and benefits to United States populations and businesses. Further, together, the two Executive Orders set the following requirements: quantify costs and benefits where the new regulation creates a change in current practice; qualitatively describe costs and benefits; choose approaches that maximize net benefits; and support regulations that protect public health and safety. HHS/CDC has analyzed the NPRM as required by these Executive Orders and has determined that it is consistent with the principles set forth in the Executive Orders and the Regulatory Flexibility Act, as amended by the Small Business Regulatory Enforcement Fairness Act (SBREFA).

Executive Order 12866, as reaffirmed by E.O. 13563 and E.O. 14094, provides that the Office of Information and Regulatory Affairs (OIRA) in the Office of Management and Budget will review all significant rules. OIRA has determined that this rule is significant.

Executive Order 14094 reaffirms the principles of E.O. 12866 and E.O. 13563 and states that regulatory analysis should facilitate agency efforts to develop regulations that serve the public interest, advance statutory objectives, and are consistent with E.O. 12866, E.O. 13563, and the Presidential Memorandum of January 20, 2021 (Modernizing Regulatory Review). Regulatory analysis, as practicable and appropriate, shall recognize distributive impacts and equity, to the extent permitted by law. We have developed this proposed rule in a manner consistent with these requirements. E.O. 13563 emphasizes further that regulations must be based on the best available science and that the rulemaking process must allow for public participation and an open exchange of ideas. We have developed this proposed rule in a manner consistent with these requirements. In administering the Federal Select Agent Program (FSAP), HHS, along with USDA, regularly interact with the affected registered entities via email, phone, online webinars, and interactions through the eFSAP information system and through registered entity designated points of contact. All proposed changes are being proposed as a direct result of entity questions received and/or interaction with registered entities who have contacted FSAP when they had questions or regulatory interpretation requests. Therefore, HHS/CDC believes this proposed rule serves the public interest. Additionally, HHS/CDC further encourages public participation and will inform registered entities of this proposed rule via a Select Agent (SA) Gram to ensure they are aware that they have a chance to provide public

comments. The proposed rule will also be communicated to the general public via a GovD message to ensure the public has a chance to review and provide comments. The Federal Select Agent Program website (*www.selectagents.gov*) will also be updated to share what the proposed changes are and will provide a link to web visitors so that they can review and provide comments on our **Federal Register** notice. Lastly, outreach notes summarizing the proposed rule will be emailed directly to national partner organizations (The Association of Public Health Laboratories, American Society for Microbiology, American Biological Safety Association, etc.) so that they can share among their constituents.

We have prepared an economic analysis for this NPRM. The economic analysis provides a cost-benefit analysis, as required by Executive Order 12866. This regulatory flexibility analysis also examines the potential economic effects of this rule on small entities, as required by the Regulatory Flexibility Act. The economic analysis is summarized below. Copies of the full analysis are available at the Supporting Materials tab of the docket, or at *www.select agents.gov*.

Summary of the Regulatory Impact Analysis

HHS/CDC has proposed modifications to the list of select agents and toxins as well as revisions to several of the select agent and toxin regulations. These proposed revisions to the select agent and toxin regulations will increase their usability as well as provide for enhanced program oversight. Specifically, HHS/CDC is proposing to add definitions for several terms (*Discovery, Theft, Loss, Release, Validated Removal Procedure, Verification viability testing protocol*); codify policies regarding the role of responsible officials and alternate responsible officials, conclusion of patient care, and annual internal inspections; and revise or clarify provisions related to validated inactivation procedures and viable select agent removal methods, recordkeeping, non-possession of select agents and toxins, eFSAP, registration, Tier 1 enhancements, and exclusion of naturally infected animals. HHS/CDC is also proposing to add requirements for reporting discoveries of select agents and toxins, provisions regarding effluent decontamination system, biosafety provisions for facility verification requirements for registered biosafety level 3 and animal biosafety level 3 laboratories, new requirement related to restricted experiments, as well as to correct editorial errors. These proposed changes would economically benefit producers, research and reference laboratories, and State and Federal oversight agencies, while also maintaining adequate program oversight of select agents and toxins.

Currently, there are 236 entities registered with APHIS and CDC. Of these entities, there are 13 Private entities, 30 Federal entities, 42 Commercial entities, 84 Academic entities, and 67 State entities registered with APHIS and CDC. Less than 4 percent of all firms operating within these North American Industry Classification (NAICS) categories are considered to be small entities. The NPRM will not have a significant economic impact on a substantial number of small entities.

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

The proposed amendments to the regulations will enhance the protection of human, animal, and plant health and safety. The proposal is to reduce likelihood of the accidental or intentional release of a select agent or toxin. Benefits of the rules will derive from the greater probability that a release will be prevented from occurring.

B. The Regulatory Flexibility Act (RFA), as Amended by the Small Business Regulatory Enforcement Fairness Act (SBREFA)

HHS/CDC has examined the impacts of the proposed rule under the Regulatory Flexibility Act (5 U.S.C. 601–612). Unless HHS/CDC certifies that the proposed rule is not expected to have a significant economic impact on a substantial number of small entities, the Regulatory Flexibility Act (RFA), as amended by the Small Business Regulatory Enforcement Fairness Act (SBREFA), requires agencies to analyze regulatory options that would minimize any significant economic impact of a rule on small entities. HHS/CDC certifies that this proposed rule will not have a significant economic impact on a substantial number of small entities within the meaning of the RFA.

This regulatory action is not a major rule as defined by Sec. 804 of the Small Business Regulatory Enforcement Fairness Act of 1996. This proposed rule will not result in an annual effect on the economy of $100,000,000 or more; a major increase in cost or prices; or significant adverse effects on competition, employment, investment, productivity, innovation, or on the ability of United States-based companies to compete with foreign-based companies in domestic and export markets.

C. Paperwork Reduction Act of 1995

In accordance with section 3507(d) of the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 *et seq.*), HHS/CDC has determined that the Paperwork Reduction Act does apply to information collection and recordkeeping requirements included in this rule. HHS/CDC notes that the information collection and recordkeeping requirements are already approved by the Office of Management and Budget (OMB) under OMB Control Number 0920–0576, expiration 1/31/2024. HHS/CDC will be seeking renewal of the information collection prior to the publication of the final rule. HHS/CDC will also pursue OMB approval for the proposed Form 6 through a separate process, through a standard clearance with OMB, rather than in this rulemaking.

The total estimated annualized burden for all data collection was calculated using the 2021 Annual Report of the Federal Select Agent Program available at *https://www.selectagents.gov/resources/publications/annualreport/2021.htm* or FSAP IT system and is estimated as 3,655.5 hours and includes additional 30 minutes added to the average burden per response (in hours) for the training proposal in accordance with the new mandate in the Consolidated Appropriations Act, 2023, Public Law 117–328 (division H, title II, section 2311), ''Improving Control and Oversight of Select Biological Agents and Toxins'' (Section 351A of the Public Health Service Act (42 U.S.C. 262a)) amendment of subsection (b)(1). Information will be collected through FSAP IT system, fax, email and hard copy mail from respondents.

ESTIMATED ANNUALIZED BURDEN HOURS

Section	Form name	Number of respondents	Number of responses per respondent	Average burden per response (in hours)	Total burden hours
Sections 3 & 4	Request for Exclusions	1	1	1	1
Sections 5 & 6	Form 4—Report of Identification of a Select Agent or Toxin.	917	1	1	917
Sections 5 & 6	Form 5—Request of Exemption	1	1	1	1
Section 7	Form 1—Application for Registration	5	1	5	25
Section 7	Form 1 Sec 6A—Amendment to a Certificate of Registration.	144	5	1	720
Section 9	Documentation of self-inspection	233	1	1	233
Section 10	Request for Expedited Review	1	1	30/60	1
Section 11	Security Plan	233	1	1	233
Section 12	Biosafety Plan	233	1	1	233
Section 13	Request Regarding a Restricted Experiment	3	1	2	6
Section 14	Incident Response Plan	233	1	1	233
Section 15	Training	233	1.5	1.5	339.5
Section 16	Form 2—Request to Transfer Select Agents and Toxins	229	1	1.5	380
Section 17	Records	233	1	30/60	117
Section 19	Form 3—Notification of Theft, Loss, or Release	185	1	1	185
Section 20	Administrative Review	22	1	1	22
Total					3,655.5

D. E.O. 12988: Civil Justice Reform

This rule has been reviewed under E.O. 12988, Civil Justice Reform. Once the final rule is in effect, HHS/CDC notes that: (1) All State and local laws and regulations that are inconsistent with this rule will be preempted; (2) No retroactive effect will be given to this rule; and (3) Administrative proceedings will not be required before parties may file suit in court challenging this rule.

E. E.O. 13132: Federalism

HHS/CDC has reviewed this proposed rule in accordance with Executive Order 13132 regarding Federalism and has determined that it does not have ''federalism implications.'' The rule does not ''have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government.''

In accordance with section 361(e) of the PHSA [42 U.S.C. 264(e)], nothing in this rule would supersede any provisions of State or local law except to the extent that such a provision conflicts with this rule.

F. Plain Language Act of 2010

Under the Plain Language Act of 2010 (Pub. L. 111–274, October 13, 2010), executive Departments and Agencies are required to use plain language in documents that explain to the public how to comply with a requirement the Federal Government administers or enforces. HHS/CDC has attempted to use plain language in promulgating this rule consistent with the Federal Plain Writing Act guidelines.

VI. References

Abdu F. Pathogenic Rickettsiae as Bioterrorism Agents, Clinical Infectious Diseases, 45 (Supplement_1). 2007. p. S52–S55.

Adler M. et al. Toxicity of Botulinum Neurotoxin by Inhalation: Implications in Bioterrorism. In: Salem H, Katz SA, editors. Aerobiology: The Toxicology of Airborne Pathogens and Toxins. Cambridge: The Royal Society of Chemistry Press; 2016. p. 167–82.

Anderson A. et al. *Seroprevalence of Q fever in the United States, 2003–2004.* Am J Trop Med Hyg. 2009. 81: p. 691–694.

Battisti, L. et al. *Mating system for transfer of plasmids among Bacillus anthracis, Bacillus cereus, and Bacillus thuringiensis.* J Bacteriol. 1985. 162(2): p. 543–50.

Bergdoll, M. Staphylococcal intoxications, in Foodborne infections and intoxications, 2nd Edition, H. Riemann and F.L. Bryan, Editors. 1979, Academic Press.

Biodefence Modeling Parameter Review Workshop. 2013: Ventura, California.

Cataldi A., et al. *Characterization of Bacillus anthracis strains used for vaccination.* 2000. J Appl Microbiol 86: p. 648–654.

Centers for Disease Control and Prevention. 2017. *Annual U.S. Hantavirus Disease and HPS Case Fatality, 1993–2016.* Retrieved from *https://www.cdc.gov/hantavirus/surveillance/annual-cases.html.*

Centers for Disease Control and Prevention and National Institutes of Health. 2009. Biosafety in Microbiological and Biomedical Laboratories. 5th ed. Retrieved from *https://www.cdc.gov/labs/pdf/CDC-BiosafetyMicrobiologicalBiomedicalLaboratories-2009-P.PDF.*

Cross, et al. *Zoonoses under our noses.* Microbes and Infection, 2019. 21(1). *https://doi.org/10.1016/j.micinf.2018.06.001*

Cutler, S. *Q Fever.* J Infect, 2007. 54(4): p. 313–8.

De Wit, E., et al. *Foodborne transmission of Nipah virus in Syrian Hamsters.* PLoS Pathog, 2014. 10(3): p. e1004001.

Eremeeva, M. E. et al. *Typhus, Epidemic (Rickettsia prowazekii) and Rocky Mountain Spotted Fever (Rickettsia rickettsii).* Encyclopedia of Bioterrorism Defense, 2005. John Wiley & Sons, Inc.

Gardner, C., et al., *Eastern and Venezuelan equine encephalitis viruses differ in their ability to infect dendritic cells and macrophages: impact of altered cell tropism on pathogenesis.* J Virol. 2008. 82(21): p. 10634–46.

Geisbert, T., et al. *Development of an Acute and Highly Pathogenic Nonhuman Primate Model of Nipah Virus Infection.* PLoS ONE, 2010. 5(5): p. e10690.

Gidding H., et al. *Q fever seroprevalence in Australia suggests one in twenty people have been exposed.* Epidemiol Infect. 2020. 148: e18.

Godfroid, J., et al. *Brucellosis in Terrestrial Wildlife.* Rev sci tech Off int Epiz. 2013. 32(1), p. 27–42.

Green, B., et al. *Involvement of Tn4430 in transfer of Bacillus anthracis plasmids mediated by Bacillus thuringiensis plasmid pXO12.* J Bacteriol. 1989. 171(1): p. 104–13.

Gurley, E., et al. *Person-to-Person Transmission of Nipah virus in a Bangladeshi Community.* Emerg Infect Dis, 2007. 13(7): p. 1031–7.

Guzman, K.D., et al., *Biological Terrorism Modeling Parameters.* 2014, Sandia National Laboratories.

Harcourt, B., et al. *Genetic Characterization of Nipah virus, Bangladesh, 2004.* Emerg Infect Dis, 2005. 11(10): p. 1594–1597.

HHS/CDC. November 3, 2003. Possession, Use, and Transfer of Select Agents and Toxins. Interim Final Rule. *https://www.federalregister.gov/d/03-27659.*

Hossain, M., et al. *Clinical Presentation of Nipah virus Infection in Bangladesh.* Clin Infect Dis, 2008. 46(7): p. 977–84.
Institute for International Cooperation in Animal Biologics. 2004. *Typhus Fever-Rickettsia prowazekii.* Retrieved from *http://www.cfsph.iastate.edu/Factsheets/pdfs/typhus_fever.pdf.*
Ivins, B., et al. *Immunization Studies with Attenuated Strains of Bacillus anthracis.* Infect Immun, 1986. 52(2):p. 454–458.
Johnston, C., et al. *Bacterial Transformation: Distribution, Shared Mechanisms and Divergent Control.* Nature Rev. Microbiol, 2014. 12: p. 181–196.
Kersh G., et al. *Presence of Coxiella burnetii DNA in the environment of the United States, 2006 to 2008.* Appl Environ Microbiol. 2010.
Kinney, R., et al., *Attenuation of Venezuelan equine encephalitis virus strain TC–83 is encoded by the 5'-noncoding region and the E2 envelope glycoprotein.* J Virol, 1993. 67(3): p. 1269–77.
Knutsen, H., et al. *Risk to human and animal health related to the presence of 4,15-diacetoxyscirpenol in food and feed.* EFSA Jour, 2018. 16(8): p. 1–106.
Koehler, T., et al. *Bacillus subtilis (natto) plasmid pLS20 mediates interspecies plasmid transfer.* J Bacteriol. 1987. 169(11): p. 5271–8.
Kuhn, J., et al. ICTV Virus Taxonomy Profile: Filoviridae. J Gen Virol. 2019. 100(6): p. 911–912.
Lo, M., et al. *The Emergence of Nipah virus, a Highly Pathogenic Paramyxovirus.* J Clin Virol, 2008. 43(4): p. 396–400.
Luby, S., et al. *Epidemiology of Henipavirus disease in Humans.* Curr Top Microbiol Immunol, 2012. 359: p. 25–40.
Luby, S., et al. *Recurrent Zoonotic Transmission of Nipah virus into Humans, Bangladesh, 2001–2007.* Emerg Infect Dis, 2009. 15(8): p. 1229–35.
Luna, V., et al. *Bacillus anthracis Virulent Plasmid pXO2 Genes Found in Large Plasmids of Two Other Bacillus species.* J of Clinical Microbiol, 2006. 44(7): P. 2367–77.
Mathieu, C., et al. *Nonstructural Nipah Virus C Protein Regulates both the Early Host Proinflammatory Response and Viral Virulence.* Journal of Virology, 2012. 86(19): p. 10766–10775.
Olsen, S., et al. *Biosafety Concerns Related to Brucella and its Potential Use as a Bioweapon.* Applied Biosafety, 2018. 23(2): p. 77–90.
Paessler, S., et al., *Vaccines for Venezuelan equine encephalitis.* Vaccine, 2009. 27 Suppl 4: p. D80–5.
Peck, M., *Biology and genomic analysis of Clostridium botulinum.* Adv Microb Physiol, 2009. 55: p. 183–265, 320.
Pike, R. *Laboratory-Associated Infections: Summary and Analysis of 3921 Cases.* Health Lab Sci, 1976. 13(2): p. 105–14.
Puig de Centorbi, O., et al. *Selection of a Strain of Clostridium argentinense Producing High Titers of Type G Botulinal Toxin.* Zentralbl Bakteriol. 1997. 286(3): p. 413–9.
Raoult, D., et al. *Antimicrobial Therapy of Rickettsial Diseases.* Antimicrob Agents Chemother, 1991. 35(12): p. 2457–62.
Reynolds, M.G., et al., *Flying Squirrel-Associated Typhus, United States.* Emerg Infect Dis, 2003. 9(10): p. 1341–3.
Rivas, F., et al. *Epidemic Venezuelan Equine Encephalitis in La Guajira, Colombia.* J Infect Dis, 1997. 175(4): p. 828–32.
Rolain, J., et al. *Correlation Between Ratio of Serum Doxycycline Concentration to MIC and Rapid Decline of Antibody Levels during Treatment of Q Fever Endocarditis.* Antimicrob Agents Chemother, 2005. 49: p. 2673–76.
Rossi, S., et al. *Rationally Attenuated Vaccines for Venezuelan Equine Encephalitis Protect Against Epidemic Strains with a Single Dose.* Vaccines, 2020. 8(3): p. 497.
Ruhfel et al. *Interspecies transduction of plasmids among Bacillus anthracis, B. cereus, and B. thuringiensis. J Bacteriol,* 1984. 157(3): p.708–11.
Shakir, R. *Brucellosis.* Journal of the Neurological Sciences, 2021. 420(15). *https://doi.org/10.1016/j.jns.2020.117280*
Sejvar J., et al. *Long-term Neurological and Functional Outcome in Nipah virus Infection.* Ann Neurol. 2007 Sep;62(3): p. 235–42.
Seqiris Pty Ltd PV. Q–VAX, *Q Fever Vaccin*e, Consumer Medical Information, 2014.
Sobel, J. *Botulism.* Clin Infect Dis, 2005. 41(8): p. 1167–73.
Smith, D. et al. *Alphaviruses.* Clinical Virology, 3rd ed., ASM Press, 2009. pp. 1241–1274.
Spero, L. et al. *Staphylococcal enterotoxin A (SEA).* Methods Enzymol. 1981. 78(Pt A): p. 331–6.
Spickler, A. 2018. *Brucellosis.* Retrieved from *http://www.cfsph.iastate.edu/DiseaseInfo/factsheets.php.*
Thapa, M. et al. *Conotoxins and their regulatory considerations.* Reg and Tox and Pharm, 2014. 70: p. 197–202.
Walker, D. *Rickettsiae and rickettsial infections: the current state of knowledge.* Clin Infect Dis. 2007. 45 Suppl 1: p. S39–44.
Walker, D. *Principles of the Malicious Use of Infectious Agents to Create Terror—Reasons for Concern for Organisms of the Genus Rickettsia.* Rickettsiology: Present and Future Directions, 2003. 990: p. 739–742.
Walton, T., et al., *Persistence of neutralizing antibody in Equidae vaccinated with Venezuelan equine encephalomyelitis vaccine strain TC–83.* J Am Vet Med Assoc., 1972;161(8): p. 916–8.
Walton, T., et al., *Duration of immunity of horses vaccinated with strain TC–83 Venezuelan equine encephalomyelitis virus vaccine.* Proc Annu Meet U S Anim Health Assoc., 1973;77: p. 196–202.
Weaver, S., et al. *Re-emergence of Epidemic Venezuelan Equine Encephalomyelitis in South America.* Lancet, 1996. 348(9025): p. 436–40.
Weaver, S., et al., *Genetic determinants of Venezuelan equine encephalitis emergence.* Arch Virol Suppl, 2004. (18): p. 43–64.
World Health Organization, *Nipah Virus Outbreaks in the WHO South-East Asia Region.* 2017. Retrieved from *www.searo.who.int/entity/emerging_diseases/links/nipah_virus_outbreaks_sear/en/.*

List of Subjects

Biologics, Packaging and containers, Penalties, Reporting and recordkeeping requirements, Transportation.

For the reasons discussed in the preamble, HHS proposes to amend 42 CFR part 73 as follows:

PART 73—SELECT AGENTS AND TOXINS

■ 1. The authority citation for part 73 is revised to read as follows:

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

§ 73.0 [Removed]

■ 2. Remove § 73.0.
■ 3. Section 73.1 is amended by:
■ a. Adding in alphabetical order definitions for ''Discovery'', ''Loss'', ''Release'', and ''Theft'';
■ b. Revising the definition of ''Validated inactivation procedure'';
■ c. Adding in alphabetical order definitions for ''Validated removal procedure'' and ''Verification viability testing protocol''; and
■ d. Revising the definition of ''Viability testing protocol''.

The additions and revision read as follows:

§ 73.1 Definitions.

* * * * *

Discovery means the finding of a select agent or toxin by an individual or entity that is not aware of the select agent or toxin's existence. Examples include, but are not limited to, the following:

(1) A registered individual or entity finds a select agent or toxin not accounted for in their inventory; or

(2) A non-registered individual or entity finds a select agent or toxin.

* * * * *

Loss means the inability to account for a select agent or toxin known to be in the individual or entity's possession.

* * * * *

Release means any of the following:

(1) An incident resulting in occupational exposure to a select agent or toxin,

(2) An incident resulting in animal/plant exposure to a select agent or toxin,

(3) The failure of equipment used to contain a select agent or toxin such that it is reasonably anticipated that a select agent or toxin was released,

(4) The failure of or breach in personal protective equipment in the presence of a select agent or toxin, or

(5) The failure of biosafety procedures such that it is reasonably anticipated

that a select agent or toxin was outside of containment.

* * * * *

Theft means the unauthorized taking and removing of a select agent or toxin from the possession of an entity or individual.

* * * * *

Validated inactivation procedure means a procedure, whose efficacy has been confirmed by data generated from an in-house 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.

* * * * *

Validated removal procedure means a procedure, whose efficacy has been confirmed by data generated in-house from a viability testing protocol, to confirm removal of all viable select agent, or nucleic acids of any select agent virus capable of producing infectious virus.

* * * * *

Verification viability testing protocol means a protocol, used on samples that have been subjected to a validated inactivation or removal procedure, to confirm the material is free of all viable select agent, or nucleic acids of any select agent virus capable of producing infectious virus.

* * * * *

Viability testing protocol means a protocol used to confirm the efficacy of the inactivation or removal procedure by demonstrating the material is free of all viable select agent, or nucleic acids of any select agent virus capable of producing infectious virus.

* * * * *

■ 5. Section 73.2 is revised to read as follows:

§ 73.2 Purpose and scope.

(a) This part implements the provisions of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 and the Public Health Service Act, 42 U.S.C. 262a, as amended, setting forth the requirements for possession, use, and transfer of select agents and toxins. The biological agents and toxins listed in this part have the potential to pose a severe threat to public health and safety, to animal health, or to animal products. Overlap select agents and toxins are subject to regulation by both CDC and APHIS.

(b) Any individual or entity in possession of a select agent or toxin, for which an exclusion or exemption listed in this part does not apply, and that is not included on a certificate of registration issued by the HHS Secretary or Administrator for that individual or entity, must immediately report such possession to either the HHS Secretary or Administrator by the submission of an APHIS/CDC Form 6.

■ 6. Section 73.3 is amended by:

■ a. Revising paragraphs (b), (d)(1), and (d)(4) through (6);

■ b. Redesignating paragraphs (d)(7) through (11) as paragraphs as (d)(8) through (12), respectively.

■ c. Adding new paragraph (d)(7);

■ d. In newly redesignated paragraph (d)(8) introductory text, removing the text ''100 mg of Conotoxins'' and adding in its place the text ''200 mg of Conotoxins'';

■ e. In newly redesignated paragraph (d)(12) by removing the text ''of the conclusion of patient care'' and adding in its place ''from when the individual has been released from the medical facility where treatment was being provided'';

■ f. In paragraph (e)(1), removing the text ''National Select Agent Registry website'' and adding in its place ''Federal Select Agent Program website'';

■ g. In paragraph (f)(3)(i), removing the text ''*Bacillus cereus* Biovar *anthracis,* Botulinum neurotoxins, Botulinum neurotoxin producing species of *Clostridium,* Ebola viruses, *Francisella tularensis,* Marburg virus, Variola major virus (Smallpox virus), Variola minor (Alastrim), or *Yersinia pestis*'' and adding in its place ''Tier 1 agents and toxins'' and removing the text ''telephone, facsimile, or email'' and adding in its place the text ''eFSAP information system, telephone, or email'';

■ h. In paragraph (f)(3)(iii), adding the text ''not submitted through eFSAP information system'' between the words ''APHIS/CDC Form 4'' and ''must''; and

■ k. In paragraph (f)(4), adding the text ''not submitted through eFSAP information system'' between the words ''form'' and ''must''.

The revisions and additions read as follows:

§ 73.3 HHS select agents and toxins.

* * * * *

(b) HHS select agents and toxins:

Abrin
Bacillus cereus Biovar *anthracis* *
Botulinum neurotoxins *
Botulinum neurotoxin producing species of *Clostridium*
Conotoxins (Short, paralytic alpha conotoxins containing the following amino acid sequence $X_1CCX_2PACGX_3X_4X_5X_6CX_7$) [1]
Coxiella burnetii
Crimean-Congo hemorrhagic fever virus [2]
Diacetoxyscirpenol
Eastern equine encephalitis virus [2]
Ebolavirus * [2]
Francisella tularensis *
Lassa fever virus [2]
Lujo virus [2]
Marburg virus * [2]
Mpox virus (clade I) [2]
Reconstructed replication competent forms of the 1918 pandemic influenza A virus containing any portion of the coding regions of all eight gene segments (Reconstructed 1918 influenza A virus) [2]
Ricin
Rickettsia prowazekii
Severe acute respiratory syndrome coronavirus (SARS-CoV) [2]
Saxitoxin
South American hemorrhagic fever viruses [2]:
  Chapare
  Guanarito
  Junin
  Machupo
  Sabia
Staphylococcal enterotoxins (subtypes A,B,C,D,E)
T–2 toxin
Tetrodotoxin
Tick-borne encephalitis virus [4]
  Far Eastern subtype
  Siberian subtype
Kyasanur Forest disease virus [2]
Omsk haemorrhagic fever virus [2]
Variola major virus (Smallpox virus) * [2]
Variola minor virus (Alastrim) * [2]
Yersinia pestis *

[1] C = Cysteine residues are all present as disulfides, with the 1st and 3rd Cysteine, and the 2nd and 4th Cysteine forming specific disulfide bridges; The consensus sequence includes known toxins a-MI and a-GI (shown above) as well as a-GIA, Ac1.1a, a-CnIA, a-CnIB; X1 = any amino acid(s) or Des-X; X2 = Asparagine or Histidine; P = Proline; A = Alanine; G = Glycine; X3 = Arginine or Lysine; X4 = Asparagine, Histidine, Lysine, Arginine, Tyrosine, Phenylalanine or Tryptophan; X5 = Tyrosine, Phenylalanine, or Tryptophan; X6 = Serine, Threonine, Glutamate, Aspartate, Glutamine, or Asparagine; X7 = Any amino acid(s) or Des X and; ''Des X'' = ''an amino acid does not have to be present at this position.'' For example, if a peptide sequence were XCCHPA then the related peptide CCHPA would be designated as Des-X.

[2] Please refer to *https://www.selectagents.gov* for current information on historical or proposed nomenclature for the HHS select agents on the list.

* * * * *

(d) * * *

(1) * * * Except for:

(i) Any animal which is naturally infected with a select agent from its natural environment to an artificially

established environment for the purpose of the intentional exposure or introduction of a select agent to a naïve or experimental animal; or

(ii) Any animal which is naturally infected with a select agent for the purpose of the intentional exposure or introduction of a select agent to the naïve or experimental animal is placed with a naïve animal in their natural environment.

* * * * *

(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, provided that:

(i) In-house validation of the inactivation procedure is completed prior to use;

(ii) A certificate of inactivation has been generated in accordance with § 73.17(a)(8);

(iii) For use of a select agent surrogate to validate an inactivation procedure:

(A) Select agent surrogates must be known to possess equivalent properties with respect to inactivation;

(B) If there are known variations in the resistance of a select agent to an inactivation procedure, including strain to strain, then an inactivation procedure must also be validated using the most resistant select agent surrogate.

(iv) For use of a whole tissue or homogenized tissue surrogate to validate a chemical inactivation procedure for other tissues, including those in other animal models:

(A) All standardized conditions must be held constant, such as the select agent used, tissue volume, and ratio of tissue to volume of inactivating chemical;

(B) A safety margin must be incorporated into the final chemical inactivation procedure to ensure the effective inactivation of the select agent;

(C) The tissue surrogate must meet the following criteria:

(*1*) The tissue is expected to have the highest concentration of the specific select agent to be inactivated; or

(*2*) The concentration of the select agent in the tissue must be determined and this select agent concentration must not be exceeded when applying the validated inactivation procedure on subsequent tissue samples.

(5) Any select agent or regulated nucleic acids that can produce infectious forms of any select agent virus contained in a formalin-fixed paraffin-embedded (FFPE) tissue if the FFPE process used is a recognized procedure for that particular select agent or regulated nucleic acids.

(6) Material containing a select agent that is subjected to a validated viable select agent removal procedure that has rendered the material free of all viable select agent provided that:

(i) In-house validation of the viable select agent removal procedure is completed prior to use;

(ii) A certificate of viable select agent removal has been generated in accordance with § 73.17(a)(8);

(iii) For use of a surrogate to validate a viable select agent removal procedure, only surrogates known to possess equivalent properties with respect to removal are used.

(A) Select agent surrogates must be known to possess equivalent properties with respect to inactivation.

(B) If there are known variations in the resistance of a select agent to an inactivation procedure, including strain to strain, then an inactivation procedure must also be validated using the most resistant select agent surrogate.

(iv) A portion of each subsequent sample has been subjected to a verification viability testing protocol to ensure that the validated viable select agent removal procedure has rendered the material free of all viable select agent.

(7) 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 validated viable select agent removal procedure that removes all viable select agent cells, spores, or virus particles if the material is determined by the HHS Secretary 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 or CDC. A written decision granting or denying the request will be issued.

* * * * *

■ 7. Section 73.4 is amended by:

■ a. Revising paragraphs (b), (d)(1), and (d)(4) through (6);

■ b. Redesignating paragraphs (d)(7) through (9) as paragraphs (d)(8) through (d)(10), respectively.

■ c. Adding new paragraph (d)(7);

■ d. In newly redesignated paragraph (d)(9), removing the text ''of the conclusion of patient care'' and adding in its place ''from when the individual has been released from the medical facility where treatment was being provided'';

■ e. Revising newly redesignated paragraph (d)(10);

■ f. In paragraph (e)(1), removing the text ''National Select Agent Registry website'' and adding in its place ''Federal Select Agent Program website'';

■ g. In paragraph (f)(3)(i), removing the text ''*Bacillus anthracis, Burkholderia mallei* and *Burkholderia pseudomallei*'' and adding in its place ''Tier 1 agents'' and removing the text ''telephone, facsimile, or email'' and adding in its place the text ''eFSAP information system, telephone, or email'';

■ h. In paragraph (f)(3)(iii), adding the text ''not submitted through eFSAP Information System'' between the text ''APHIS/CDC Form 4'' and ''must'';

■ i. In paragraph (f)(4), adding the text ''not submitted through eFSAP information system'' between the words ''form'' and ''must''.

The revisions and addition read as follows:

§ 73.4 Overlap select agents and toxins.

* * * * *

(b) Overlap select agents and toxins:

Bacillus anthracis *
Bacillus anthracis Pasteur strain
Burkholderia mallei *
Burkholderia pseudomallei *
Hendra virus
Nipah virus *
Rift Valley fever virus
Venezuelan equine encephalitis virus

* * * * *

(d) * * *

(1) Except for:

(i) Any animal which is naturally infected with a select agent from its natural environment to an artificially established environment for the purpose of the intentional exposure or introduction of a select agent to a naïve or experimental animal; or

(ii) Any animal which is naturally infected with a select agent for the purpose of the intentional exposure or introduction of a select agent to the naïve or experimental animal is placed with a naïve animal in their natural environment.

* * * * *

(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, provided that:

(i) In-house validation of the inactivation procedure is completed prior to use;

(ii) A certificate of inactivation has been generated in accordance with § 73.17(a)(8);

(iii) For use of a select agent surrogate to validate an inactivation procedure:

(A) Select agent surrogates must be known to possess equivalent properties with respect to inactivation;

(B) If there are known variations in the resistance of a select agent to an inactivation procedure, including strain to strain, then an inactivation procedure

must also be validated using the most resistant select agent surrogate;

(iv) For use of a whole tissue or homogenized tissue surrogate to validate a chemical inactivation procedure for other tissues, including those in other animal models:

(A) All standardized conditions must be held constant, such as the select agent used, tissue volume, and ratio of tissue to volume of inactivating chemical;

(B) A safety margin must be incorporated into the final chemical inactivation procedure to ensure the effective inactivation of the select agent;

(C) The tissue surrogate must meet the following criteria:

(*1*) The tissue is expected to have the highest concentration of the specific select agent to be inactivated; or

(*2*) The concentration of the select agent in the tissue must be determined and this select agent concentration must not be exceeded when applying the validated inactivation procedure on subsequent tissue samples.

(5) Any select agent or regulated nucleic acids that can produce infectious forms of any select agent virus contained in a FFPE tissue if the FFPE process used is a recognized procedure for that particular select agent or regulated nucleic acids.

(6) Material containing a select agent that is subjected to a validated viable select agent removal procedure to ensure that the validated viable select agent removal procedure has rendered the material free of all viable select agent except for:

(i) In-house validation of the viable select agent removal procedure is completed prior to use;

(ii) A certificate of viable select agent removal has been generated in accordance with § 73.17(a)(8);

(iii) For use of a surrogate to validate a viable select agent removal procedure, only surrogates known to possess equivalent properties with respect to removal are used; and

(iv) A portion of each subsequent sample has been subjected to a verification viability testing protocol to ensure that the validated viable select agent removal procedure has rendered the material free of all viable select agent.

(7) 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 validated viable select agent removal procedure that removes all viable select agent cells, spores, or virus particles if the material is determined by the HHS Secretary 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 or CDC. A written decision granting or denying the request will be issued.

* * * * *

■ 8. Section 73.5 is amended as follows:

■ a. By revising paragraph (a)(1);

■ b. In paragraph (a)(3) by removing the text ''delivery of patient (*i.e.,* human) care by health care professionals has concluded'' and adding in its place ''the individual has been released from the medical facility where treatment was being provided''.

■ c. By revising paragraph (a)(4)(i);

■ d. In paragraph (a)(4)(iv) by adding the text ''not submitted through eFSAP Information System'' between the text ''APHIS/CDC Form 4'' and ''must'';

■ e. In paragraph (b) introductory text by removing the article ''a'' and adding in its place the article ''an'' before ''HHS'';

■ f. By revising paragraph (b)(1); and

■ g. In the last sentence of paragraph (b)(3) by adding the text ''not submitted through eFSAP Information System'' between the words ''form'' and ''must''.

The revisions read as follows:

§ 73.5 Exemptions for HHS select agents and toxins.

(a) * * *

(1) Unless directed otherwise by the HHS Secretary, within seven calendar days after identification of the select agent or toxin (except for Botulinum neurotoxin), or within 30 calendar days after identification of Botulinum neurotoxin, the select agent or toxin is transferred in accordance with § 73.16 or destroyed on-site by a recognized sterilization process or inactivated for future use in accordance with section 73.3 (d)(4).

* * * * *

(4) The identification of the agent or toxin is reported to CDC or APHIS, the specimen provider, and to other appropriate authorities when required by Federal, State, or local law through the eFSAP information system, telephone, or email. This report must be followed by submission of APHIS/CDC Form 4 to APHIS or CDC within seven calendar days after identification.

(i) The identification of HHS Tier 1 select agents or toxin must be immediately reported through the eFSAP information system, telephone, or email. This report must be followed by submission of APHIS/CDC Form 4 within seven calendar days after identification.

* * * * *

(b) * * *

(1) Unless directed otherwise by the HHS Secretary, within 90 calendar days of receipt, the select agent or toxin is transferred in accordance with § 73.16 or destroyed on-site by a recognized sterilization process or inactivated for future use in accordance with § 73.3(d)(4).

* * * * *

■ 9. Section 73.6 is amended as follows:

■ a. By revising paragraphs (a) introductory text and (a)(1);

■ b. In paragraph (a)(3) by removing the text ''delivery of patient care by health care professionals has concluded'' and adding in its place ''the individual has been released from the medical facility where treatment was being provided'';

■ c. By revising paragraph (a)(4)(i);

■ d. In paragraph (a)(4)(iv) by adding the text ''not submitted through eFSAP information system'' between ''APHIS/CDC Form 4'' and ''must'';

■ e. By revising paragraph (b)(1); and

■ f. In the last sentence of paragraph (b)(3) by adding the text ''not submitted through eFSAP information system'' between the words ''form'' and ''must''.

The revisions read as follows:

§ 73.6 Exemptions for overlap select agents and toxins.

(a) Clinical or diagnostic laboratories and other entities that possess, use, or transfer an overlap 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 HHS Secretary or Administrator, within seven calendar days after identification, the select agent or toxin is transferred in accordance with § 73.16 or 9 CFR 121.16 or destroyed on-site by a recognized sterilization process, or inactivated for future use in accordance with § 73.4(d)(4),

* * * * *

(4) The identification of the agent or toxin is reported to CDC or APHIS, the specimen provider, and to other appropriate authorities when required by Federal, State, or local law through the eFSAP information system, telephone, or email. This report must be followed by submission of APHIS/CDC Form 4 to APHIS or CDC within seven calendar days after identification.

(i) The identification of overlap Tier 1 select agents or toxin must be immediately reported through the eFSAP information system, telephone, or email. This report must be followed by submission of APHIS/CDC Form 4

within seven calendar days after identification.

* * * * *

(b) * * *

(1) Unless directed otherwise by the HHS Secretary or Administrator, within 90 calendar days of receipt, the select agent or toxin is transferred in accordance with § 73.16 or 9 CFR part 121.16 or destroyed on-site by a recognized sterilization process or inactivated for future use in accordance with § 73.4 (d)(4),

* * * * *

■ 10. Section 73.7 is amended as follows:

■ a. In paragraph (f) by removing ''the relevant page(s) of'' and adding in its place ''information related to'';

■ b. By revising paragraph (g);

■ c. In paragraph (i) by removing the word ''may'' and adding in its place the word ''must'' and by removing the word ''circumstances'' and adding in its place the phrase ''the possession and use of the select agents and toxins''; and

■ d. In paragraph (i)(1) by removing ''the relevant page(s) of'' and adding in its place ''information related to''.

The revision reads as follows:

§ 73.7 Registration and related security risk assessments.

* * * * *

(g) The issuance of a certificate of registration may be contingent upon inspection and submission of additional information to include any or all of the following: the security plan, biosafety plan, incident response plan, or any other information related to the requirements of this part.

* * * * *

■ 11. Section 73.9 is amended as follows:

■ a. By redesignating paragraphs (a)(5) through (9) as paragraphs as (a)(6) through (10);

■ b. By adding new paragraph (a)(5);

■ c. By revising newly redesignated paragraphs (a)(7), (9), and (10);

■ d. In paragraph (b) by adding a new second sentence;

■ e. By revising paragraph (c)(1); and

■ f. In the last sentences of paragraphs (c)(2) and (d) by adding the phrase ''not submitted through eFSAP information system'' between the words ''form'' and ''must''.

The addition and revision read as follows:

§ 73.9 Responsible Official.

* * * * *

(a) * * *

(5) Not be approved as Responsible Official or alternate Responsible Official at another registered entity,

* * * * *

(7) Ensure that annual inspections are conducted for each registered space to determine compliance with the requirements in accordance with the regulations of this part. The results of each inspection must be documented, and any deficiencies identified during an inspection must be corrected and the corrections documented. The annual inspection must address whether:

(i) The entity's biosafety/biocontainment plan is being effectively implemented, as outlined in § 73.12.

(ii) The entity's security plan is being effectively implemented, as outlined in § 73.11.

(iii) The entity's incident response plan is implemented to ensure whether the entity is able to respond, as outlined in § 73.14.

(iv) Each individual with access approval from the HHS Secretary or Administrator has received the appropriate training as outlined in § 73.15.

* * * * *

(9) Investigate to determine the reason for any failure of a validated inactivation or validated viable select agent removal procedure to render material free from viable select agent. If the Responsible Official is unable to determine the cause of the failure from a validated inactivation or validated viable select agent removal procedure or receives a report of any inactivation failure after the movement of material to another location, the Responsible Official must report immediately through the eFSAP information system, telephone or email the inactivation or viable select agent removal procedure failure to CDC or APHIS.

(10) Review each of the entity's validated select agent inactivation procedure or validated viable select agent removal procedure and ensure they are revised as necessary. The review must be conducted annually or after any change in Principal Investigator, change in the validated inactivation or validated viable select agent removal procedure, or failure of the validated inactivation or validated viable select agent removal procedure. The review must be documented, and training must be conducted if there are any changes to the validated select agent inactivation or validated viable select agent removal procedure, or viability testing protocol.

(b) * * * An alternate Responsible Official can serve at multiple registered entities. * * *

(c) * * *

(1) The identification of any Tier 1 agents or toxins must be immediately reported through the eFSAP information system, telephone, or email. The final disposition of the agent or toxin must be reported by submission of APHIS/CDC Form 4 within seven calendar days after identification (except for Botulinum neurotoxin and/or Staphylococcal enterotoxin (Subtypes A–E)), which is within 30 calendar days after identification). A copy of the completed form not submitted through eFSAP information system must be maintained for three years.

* * * * *

§ 73.10 [Amended]

■ 12. Section 73.10 is amended in paragraph (c) by removing the words ''to select agents or toxins'' and adding in their place ''access approval from the HHS Secretary or Administrator''.

■ 13. Section 73.11 is amended as follows:

■ a. By redesignating paragraphs (c)(9) and (10) as paragraphs (c)(10) and (11);

■ b. By adding a new paragraph (c)(9);

■ c. In paragraph (d)(4) by removing the text ''the area where select agents or toxins are used or stored'' and adding in its place ''registered space'';

■ d. In paragraph (f) introductory text by removing the word ''possessing'' and adding in its place ''registered for'';

■ e. In paragraph (f)(1) by removing the words ''will have'' and adding in their place ''are registered for'';

■ f. By revising paragraph (f)(4)(iii); and

■ g. By removing paragraph (g) and redesignating paragraph (h) as paragraph (g).

The addition and revision read as follows:

§ 73.11 Security.

* * * * *

(c) * * *

(9) Describe procedures to prevent the theft, loss, or unauthorized access to a select agent or toxin from an effluent decontamination system originating from a registered laboratory.

* * * * *

(f) * * *

(4) * * *

(iii) Procedures for screening visitors, their property, and, where appropriate, vehicles at entry and exit points to registered space based on the entity's site-specific risk assessment;

* * * * *

■ 14. Section 73.12 is amended as follows:

■ a. In paragraphs (c)(1) and (2) by removing the words ''National Select Agent Registry website'' and adding in their place ''Federal Select Agent Program website'';

■ b. By revising paragraph (d); and

■ c. By adding paragraphs (f), (g), and (h).

The revision and additions read as follows:

§ 73.12 Biosafety.

* * * * *

(d) The biosafety plan must include an occupational health plan for individuals listed on the individual or entity's registration for access to Tier 1 select agents and toxins, and those individuals must be enrolled in the occupational health plan.

* * * * *

(f) When an effluent decontamination system is used, the plan must provide for verification that the liquid waste generated from registered space is sufficiently treated to prevent the release of a select agent or toxin prior to discharge of the waste from the facility.

(1) For a new effluent decontamination system, verification is required before initial use.

(2) For an effluent decontamination system in place, verification is required at least once every 12 months and following any major change to the effluent decontamination system.

(3) The verification must be documented.

(g) When an effluent decontamination system is used, the plan must provide that monthly routine maintenance is conducted of the effluent decontamination system, including at a minimum verification that:

(1) Alarms are functioning according to established specifications;

(2) Piping, pumps, valves, and tanks are not leaking; and

(3) Methods used to monitor and record performance measurements and are functioning according to established specifications.

(h) An individual or entity must document every 12 months the following facility verification requirements for registered biosafety level 3 and animal biosafety level 3 laboratories.

(1) Accuracy of devices that monitor directional air-flow;

(2) Confirmation that decontamination systems (*e.g.,* autoclave, room decontamination systems, digesters, liquid effluent decontamination systems) are operating to ensure the containment of the select agent and toxin;

(3) Confirmation that systems are in place to monitor, maintain and validate performance of mechanical systems to ensure that airflows and differential pressures are appropriate to maintain containment during normal/operational conditions;

(4) Verification that the facility mechanical, electrical, and drain waste and ventilation systems responsible for containment are inspected, maintained, and function as designed manufacturer specifications;

(5) Verification that the facility systems perform as intended in response to failure conditions as defined and tested during commissioning to prevent the release of select agent or toxin and verify secondary containment:

(i) Evaluate using work objectives, use of space, and facility infrastructure systems against the verified original design and standards (*e.g.,* Biosafety in Microbiological and Biomedical Laboratories, NIH Design Requirements Manual).

(ii) Implement controls and alarms to identify and alert personnel when systems fail, malfunction, or are unable to maintain containment during such an event.

(6) Certification of laboratory ventilation system HEPA filters, if present;

(7) Confirmation that room integrity has been evaluated and repairs are addressed (*e.g.,* sealed penetrations);

(8) Primary containment equipment is certified based on manufacturer's specifications (or recommendations) (*e.g.,* biological safety cabinets, flexible film isolators, animal caging);

(9) Seals on centrifuges not used in primary containment have been checked and replaced if needed; and

(10) Showers, eye wash stations, and hands-free sinks are operating properly.

§ 73.13 [Amended]

■ 15. Section 73.13 is amended in paragraph (a) introductory text by adding ''or transfer'' after ''possess''.

■ 16. Section 73.14 is amended as follows:

■ a. In paragraph (b) by adding the words ''the failure of an effluent decontamination system resulting in a release of a select agent or toxin;'' after ''a select agent or toxin;'';

■ b. By revising paragraph (c); and

■ c. In paragraph (e) introductory text by removing the words ''Entities with'' and adding in their place ''An individual or entity registered for''.

The revision reads as follows:

§ 73.14 Incident response.

* * * * *

(c) The response procedures must account for hazards associated with the select agent or toxin and appropriate actions to contain such select agent or toxin in registered space including any animals (including arthropods) or plants intentionally or accidentally exposed to or infected with a select agent, or an effluent decontamination system originating from registered space.

* * * * *

■ 17. Section 73.15 is amended as follows:

■ a. By adding paragraphs (a)(3) and (4);

■ b. In paragraph (b) by removing the words ''Entities with'' and adding in their place ''An individual or entity registered for''; and

■ c. By revising paragraph (d).

The additions and revision read as follows:

§ 73.15 Training.

* * * * *

(a) * * *

(3) Each individual not approved for access to HHS and overlap select agents and toxins by the HHS Secretary or APHIS Administrator whose responsibilities routinely place them in close proximity (*e.g.,* shared laboratory space) to areas where select agents or toxins are transferred, possessed, or used. The training must be based on the particular needs of the individual and risks associated with working near areas where select agents and toxins are handled or stored. The training must also instruct each individual on the notification requirements related to select agents and toxins. Training must be accomplished prior to the individual's close proximity to areas where select agents or toxins are handled or stored and refresher training must be provided annually.

(4) Each individual not approved for access to HHS and overlap select agents and toxins by the HHS Secretary or APHIS Administrator who performs administrative or oversight functions of the facility related to the transfer, possession or use of such agents or toxins on behalf of the entity (*e.g.,* administrative professionals, facility managers, etc.). The training must instruct each individual on the regulatory requirements relevant to their administrative or oversight functions. The training must also instruct each individual on the notification requirements related to select agents and toxins. Training must be accomplished prior to the individual performing these functions and refresher training must be provided annually.

(d) The Responsible Official must ensure a record of the training provided for each individual listed in paragraph (a) of this section is maintained. The record must include the name of the individual who received the training, the date of the training, a description of the training provided, and the means used to verify that the individual understood the training.

* * * * *

§ 73.16 Amended]

■ 18. Section 73.16 is amended in paragraph (l) introductory text by removing the article ''a'' and adding in its place the article ''an'' before ''HHS''.

■ 19. Section 73.17 is amended as follows:

■ a. By revising paragraphs (a)(1), (2), (3), and (8);

■ d. By removing the last sentence from paragraph (c); and

■ e. By adding paragraph (d).

The revisions and addition read as follows:

§ 73.17 Records.

* * * * *

(a) * * *

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

(i) The name and characteristics (*e.g.,* strain designation, GenBank Accession number);

(ii) The quantity acquired from another individual or entity (*e.g.,* containers, vials, tubes), date of acquisition, by whom, and the source;

(iii) Location where it is stored (*e.g.,* building, room number or name, and freezer identification or other storage container);

(iv) The date the agent was removed and returned, the purpose for using the agent, the name of the individual who removed and returned the agent, and when applicable, date of final disposition of the agent and by whom;

(v) Records created under § 73.16;

(vi) For intra-entity transfers (sender and the recipient are covered by the same certificate of registration), name of the select agent, the date of the transfer, the number of items transferred, the name of the sender, and the name of the recipient; and

(vii) Records created under § 73.19.

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

(3) Accurate, current inventory for each toxin held, including:

(i) The name and characteristics;

(ii) The quantity acquired from another individual or entity (*e.g.,* containers, vials, tubes, volume including concentration), date of acquisition, by whom, and the source;

(iii) The initial and current amount (*e.g.,* milligrams, milliliters, grams);

(iv) Location where the toxin is stored (*e.g.,* building, room number or name, and freezer identification or other storage container);

(v) When the toxin was accessed, the name of the toxin, the location where the toxin was accessed, the date the toxin was accessed, the purpose for accessing the toxin, the name of the individual accessing the toxin, the date the toxin was returned back to storage, the name of the individual returning the toxin back to storage, and date of final disposition of the toxin and by whom;

(vi) Records created under § 73.16;

(vii) For intra-entity transfers (sender and the recipient are covered by the same certificate of registration), name of the toxin, the date of the transfer, the number of vials transferred, the date of transfer, the name of the sender, and the name of the recipient; and

(viii) Records created under § 73.19.

* * * * *

(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 validated viable select agent removal procedure:

(i) A written description of the validated inactivation procedure or validated viable select agent removal procedure 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's Responsible Official involving a validated inactivation or validated viable select agent removal failure and the corrective actions taken;

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

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

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

(vii) A signed certificate. The certificate must:

(A) Include the date(s) the validated inactivation or validated viable select agent removal was completed;

(B) Include the validated inactivation procedure or validated viable select agent removal procedure used;

(C) Include the name of the principal investigator;

(D) Include an attestation statement certifying that the information on the certificate is true, complete, and accurate, and that the validated inactivation or validated viable select agent removal was performed as described in paragraph (a)(8)(i) of this section;

(E) Be signed by the principal investigator or designee within 7 days after completion of the validated inactivation or validated viable select agent removal. Such designee must be listed on the entity's registration and have the knowledge and expertise to provide scientific and technical direction regarding the validated inactivation procedure or the validated viable select agent removal procedure to which the certificate refers;

(F) Be maintained for as long as the material is in the possession of the registered individual or entity plus an additional 3 years;

(G) A copy of the certificate must accompany all transfers of inactivated or select agent removed material, including intra-entity transfers.

* * * * *

(d) All records created in accordance with the regulations of this part must be maintained for 3 years unless otherwise stated.

§ 73.19 [Amended]

■ 20. Section 73.19 is amended in paragraphs (a)(1) introductory text and (b)(1) introductory text by adding ''eFSAP information system,'' before the word ''telephone'' and removing the word ''email'' and adding in its place ''email''.

Dated: January 22, 2024.

Xavier Becerra,

Secretary, Department of Health and Human Services.

[FR Doc. 2024–01513 Filed 1–26–24; 8:45 am]

BILLING CODE 4163–18–P