United States Department of Agriculture

Animal and Plant Health Inspection Service

Regulatory Impact Analysis & Initial Regulatory Flexibility Analysis

Proposed Rule

[APHIS-2009-0070]
RIN 0579-AD09

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

United States Department of Health and Human Services

Centers of Disease Control and Prevention

[CDC-2011-0012]
RIN 0920-AA34

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

July 2011

Summary

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

The *Public Health Security and Bioterrorism Preparedness and Response Act of 2002* (Pub. L. No. 107-188) (the Act) provides for the regulation of certain biological agents and toxins that have the potential to pose a severe threat to both human and animal health, to plant health, or to animal and plant products. The Animal and Plant Health Inspection Service (APHIS) and the Centers for Disease Control and Prevention (CDC) have the primary responsibility for implementing the provisions of the Act within the Department of Agriculture (USDA) and for the Department of Health and Human Services (HHS), respectively. Within APHIS, Veterinary Services (VS) select agents and toxins are those that have been determined to have the potential to pose a severe threat to animal health or animal products, and Plant Protection and Quarantine (PPQ) select agents and toxins are those that have been determined to have the potential to pose a severe threat to plant health or plant products. HHS select agents and toxins are those that have been determined to have the potential to pose a severe threat to human health. APHIS and CDC coordinate regulatory activities for overlap select agents and toxins that have been determined to pose a severe threat to human and to animal health or animal products.

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

In addition, we are proposing several amendments to the regulations, including the addition of definitions and clarification of language concerning security, training, biosafety/biocontainment, and incident response. These changes would increase the applicability and effectiveness of the select agent regulations and provide for enhanced program oversight.

This rule would update the APHIS, CDC, and overlap select agent and toxin lists. The regulation of select agents and toxins is intended to prevent their misuse and thereby reduce the potential for those pathogens to harm humans, animals, animal products, plants or plant products in the United States. Should any select agent or toxin be intentionally or unintentionally released into the environment, the consequences would be significant. Consequences could include disruption of markets, difficulties in sustaining an adequate food and fiber supply, and the potential spread of disease infestations over large areas. The entities most likely to be affected by this rule would be those laboratories and other institutions conducting research and related activities that involve the use of the newly categorized Tier 1 select agents and toxins. The

impact of the changes to the regulations is expected to be minimal, however. Based on information obtained through site-specific inspections, we believe that very few entities would incur significant costs for compliance. Many of the proposed changes to the regulations would impose an added cost of the time spent on documenting measures already required for compliance, with respect to security, biocontainment/biosafety, and incident response plans, information security, and ongoing background checks. While the total costs imposed by the proposed regulations are estimated to range between $5.30 million and $6.95 million, including those costs to government, we believe many of these costs are currently incurred by affected entities as generally recognized practices. Costs actually incurred would depend upon the extent to which current facility practices will need to be optimized based on the proposed requirements. The expected benefits of strengthened safeguards against the costs associated with unintentional or deliberate release of select agents or toxins would greatly exceed the estimated costs of the proposed measures. The costs associated with a single outbreak have been known to exceed $100 million as outlined in the Regulatory Impact Analysis. Deliberate introduction greatly increases the probability of a select agent or toxin becoming established and causing wide-ranging and devastating impacts on an economy, loss of market access for consumer goods and services, disruption to society, and diminished confidence in public and private institutions.

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

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Introduction and Overview of the Action

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

Because of its size and complexity, the U.S. food and agriculture system is vulnerable to deliberate attacks, particularly from foreign diseases that do not occur domestically. The U.S. livestock industry, with revenues of approximately $150 billion annually, is extremely vulnerable to a host of highly infectious and often contagious biological agents that have never existed in the United States or have been eradicated. Many animal-targeted agents could simply be point-introduced into herds without immediate detection. Given the increasing concentration and specialization in the livestock industries, the introduction of a VS select agent could cause the immediate halt of movement and export of vast quantities of U.S. livestock and livestock products. Crops, too, are vulnerable. They are grown over very large areas (there were more than 406 million acres of cropland in the United States in 2007, for example), exacerbating difficulties in surveillance and monitoring.[1]

Impacts of the October 2001 anthrax attacks provide an example of the costs that the regulation would help to prevent. The anthrax attacks caused 5 fatalities and 17 illnesses, disrupted business and government activities, closed substantial parts of the postal service, and caused widespread apprehension and changes in behavior. Costs included more than $23 million

[1] USDA NASS. 2007 Census of Agriculture, Table 1.
http://www.agcensus.usda.gov/Publications/2007/Full_Report/Volume_1,_Chapter_1_US/st99_1_001_001.pdf

to decontaminate one Senate office building, approximately $2 billion in revenues lost to the postal service, and as much as $3 billion in additional costs to the postal service for cleanup of contamination and procurement of mail-sanitizing equipment.[2] Substantial costs due to lost productivity throughout the economy and from ongoing costs of the investigations into the incident are additional impacts.

Preparedness for a biological attack against people, crops or livestock is complicated by the large number of potential agents, the long incubation periods of some agents, and the potential for secondary transmission. All of these factors make vital the prevention of the misuse of biological agents and toxins through registration, biocontainment/biosafety, adequate security measures, and the availability of incident response capabilities.

The *Public Health Security and Bioterrorism Preparedness and Response Act of 2002* provides for the regulation of certain biological agents[3] and toxins[4] that have the potential to pose a severe threat to both human and animal health, to plant health, or to animal and plant products. The Animal and Plant Health Inspection Service (APHIS) and the Centers for Disease Control and Prevention (CDC) have the primary responsibility for implementing the provisions of the Act within the Department of Agriculture (USDA) and for the Department of Health and Human Services (HHS), respectively. Within APHIS, Veterinary Services (VS) select agents

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[2] "Regulatory Impact Analysis for 42 CFR Part 73: Possession, Use, and Transfer of Select Biological Agents and Toxins Final Rule. Centers for Disease Control and Prevention, Department of Health and Human Services. February 3, 2005."
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"The US Postal Service Response to the Threat of Bioterrorism through the Mail, " Congressional Research Service Report for Congress, February 2002. <http://www.au.af.mil/au/awc/awcgate/crs/rl31280.pdf.> Date Accessed: May 18, 2010.

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

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

and toxins[5] are those that that have been determined to have the potential to pose a severe threat to animal health or animal products, and Plant Protection and Quarantine (PPQ) select agents and toxins[6] are those that have been determined to have the potential to pose a severe threat to plant health or plant products. HHS select agents and toxins are those that have been determined to have the potential to pose a severe threat to human health.[7] APHIS and CDC coordinate regulatory activities for overlap select agents and toxins that have been determined to pose a severe threat to human and to animal health or animal products.

Sections 201 and 212(a)(2) of the Act requires a biennial review and republication of the select agent and toxin list, with revisions as appropriate in accordance with this law. This rule would implement the recommendations of the third biennial review of the list. Revision of these regulations is in compliance with the policy outlined in Executive Order 13546, "Optimizing the Security of Biological Select Agents and Toxins in the United States," that requires that the Secretaries of Health and Human Services and Agriculture publish proposed regulations to establish risk-based tiering of the select agent list, and revise the regulations, rule and guidance to accommodate a tiered select agent list no later than October 2011.

In addition, we are proposing several amendments to the regulations, including the addition of definitions and clarification of language concerning security, training, biosafety/biocontainment, and incident response. These changes would increase the transparency and effectiveness of the select agent regulations and provide for enhanced program oversight.

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[5] The current list of VS select agents and toxins can be found at 9 CFR § 121.3 (VS select agents and toxins) and 9 CFR § 121.4 (Overlap select agents and toxins).

[6] The current list of PPQ select agents and toxins can be found at 7 CFR § 331.3 (PPQ select agents and toxins).

[7] The current list of HHS select agents and toxins can be found at 42 CFR § 73.3 (HHS select agents and toxins) and 42 CFR § 73.4 (Overlap select agents and toxins).

The expected benefits and costs of the proposed rule are examined in accordance with Executive Orders 12866 and 13563.[8] The possible impacts for small entities are also considered as required by the Regulatory Flexibility Act, which requires agencies to prepare and make available for public comment an initial regulatory flexibility analysis that describes expected impacts of a proposed rule on small businesses, small organizations and small governmental jurisdictions.[9]

Regulatory Revisions of Economic Consequence

Addition of Select Agents and Toxins to HHS List

CDC is re-proposing to add Chapare to the HHS list of select agents and toxins listed in 42 CFR § 73.3. The select agents and toxins list currently includes members of the *arenaviridae* family (Junin, Machupo, Sabia, Flexal, Guanarito, and Lassa). The arenaviruses are divided into two groups: the New World or Tacaribe complex and the Old World or LCM/Lassa complex. Arenaviruses are rodent-borne viruses, some of which have been associated with large hemorrhagic fever outbreaks. Untreated case fatalities can be in excess of 30 percent. On August 19, 2009 (74 FR 41829), CDC proposed the addition of Chapare virus to the HHS list of select agents and toxins. This recently described New World arenavirus is associated with fatal hemorrhagic fever syndrome and is most closely related to Sabia virus, an HHS select agent.

CDC is also proposing to add Lujo virus, a recently described Old World arenavirus associated with an outbreak of fatal hemorrhagic fever in South Africa, to the HHS list of select agents and toxins. Lujo virus has been phylogenetically identified as an arenavirus and is related to other currently regulated arenaviruses that cause hemorrhagic fever.

[8] http://www.whitehouse.gov/omb/inforeg/eo12866.pdf; http://www.reginfo.gov/public/jsp/Utilities/EO_13563.pdf
[9] http://www.sba.gov/advo/laws/regflex.html

Removal of Plant, Animal, Human Health (and Overlap) Select Agents and Toxins

APHIS is proposing to amend the list of PPQ select agents and toxins listed in 7 CFR § 331.3 by removing Xylella fastidiosa, citrus variegated chlorosis strain, from the list as it no longer meets the criteria for or use as an agroterrorism agent and therefore no longer needs to be designated as a PPQ select agent. APHIS is also proposing to remove nine VS select agents and toxins from the list set out in § 121.3(b). Specifically, APHIS is proposing to remove the following: Akabane virus; bluetongue virus (exotic), bovine spongiform encephalopathy agent; camel pox virus; Ehrlichia ruminantium (heartwater); Japanese encephalitis virus; malignant catarrhal fever virus (Alcelaphine herpesvirus type 1); Menangle virus; and vesicular stomatitis virus (exotic): Indiana subtypes VSV–IN2, VSV–IN3.

CDC is proposing to amend the list of HHS select agents listed in 42 CFR §73.3 by removing Cercophithecine herpesvirus 1 (Herpes B virus), Coccidioides posadasii / Coccidioides immitis, the South American genotypes of eastern equine encephalitis virus, flexal virus, and tick-borne encephalitis viruses, European subtypes from the list as they no longer meet the criteria for use as a bioterrorism agent and therefore no longer need to be designated as HHS select agents.

Finally, APHIS and CDC are proposing to modify the listing for one of the overlap select agents by removing certain subtypes of Venezuelan equine encephalitis virus from the list of overlap select agents and toxins set out in 9 CFR § 121.4(b) and 42 CFR § 73.4 (b), and to clarify that only Venezuelan equine encephalitis subtypes IAB and IC would remain on the list. While the current regulations have not been shown to impede research concerning select agents and toxins listed in the Code of Federal Regulations, the removal of certain select agents and toxins may result in marginal savings of both time (the registration process) and money (the cost of compliance) for entities, thereby contributing to more efficient research processes. The overall

benefit of this provision is expected to be minimal and impact less than 3 percent of entities affected by the rule.

Reorganization of the Current List of Select Agents and Toxins and Revision of Security Requirements

APHIS and CDC are proposing to reorganize their respective lists of select agents and toxins based on the relative potential of each select agent or toxin to be misused to adversely affect human, plant, or animal health or plant or animal products. This action would establish a classification of select agents and toxins as "Tier 1" within the lists of VS, HHS, and overlap select agents and toxins.[10] All other select agents and toxins would continue to be subject to the requirements contained in 7 CFR Part 331, 9 CFR Part 121, and 42 CFR Part 73.

APHIS is proposing to list foot-and-mouth disease virus and rinderpest virus as Tier 1 VS select agents and toxins. CDC is proposing to list Ebola virus, *Francisella tularensis,* Marburg virus, Variola major virus, Variola minor virus, *Yersinia pestis,* Botulinum neurotoxin, and Botulinum neurotoxin producing species of *Clostridium* as Tier 1 HHS select agents and toxins. In addition, APHIS and CDC are proposing to list *Bacillus anthracis, Burkholderia mallei,* and *Burkholderia pseudomallei* as Tier 1 overlap select agents and toxins. The reorganization of the lists of select agents and toxins is designed to emphasize those select agents and toxins with the greatest potential for deliberate misuse that could result in devastating effects to the economy, critical infrastructure, and public confidence.

The rule would require that an entity where Tier 1 select agents and toxins are held adequately provide for an additional level of physical security of the premises. Entities possessing a Tier 1 select agent or toxin must have a security plan describing procedures for

[10] APHIS is not proposing to include PPQ select agents and toxins in this reorganization as none of the proposed Tier 1 select agents and toxins is from the plant list.

determining the suitability of persons who would have access to a Tier 1 select agent or toxin; training on policies and procedures for evaluation and reporting concerning the assessment of personnel suitability to access Tier 1 agents and toxins; and the ongoing suitability monitoring of individuals with access to Tier 1 select agents and toxins. Furthermore, entities with Tier 1 select agents and toxins must have security enhancements that contain provisions for security barriers, intrusion detection and monitoring, delay/response force, access control, and information security.

Finally, the biosafety plan must include an occupational health program for individuals with access to Tier 1 select agents and toxins, and those individuals must be enrolled in the occupational health program.

Miscellaneous Changes that May Pose Economic Impact

APHIS and CDC are proposing several additional changes to the regulations that would likely improve the transparency and effectiveness of the select agent regulations as well as provide for enhanced program oversight. These changes include various additions of definitions, as well as the clarification of language concerning security, training, biosafety, biocontainment, and incident response. Miscellaneous proposed changes to the regulations that may result in costs for affected entities are as follows:

- The responsible official would be required to possess the appropriate training or expertise to execute his/her required duties.
- Entities would be required to submit their security plan for initial registration and renewals of registration, as well as at any other time upon request.
- APHIS and CDC approval, based on a security risk assessment, to have access to select agents and toxins would be valid for a maximum of 3 years as opposed to the current standard of 5 years.

- Entities would be required to clearly state the provisions to address the safeguarding of animals or plants intentionally or accidentally exposed to or infected with select agents within their security, biosafety/biocontainment, and incident response plans.
- Information security measures, including:
    - Network connectivity monitoring,
    - Restriction of user permissions to only mission-specific files and applications,
    - Measures to prevent network infiltration by malicious code, and
    - Configuration management including regular patching and system software updates.
- Entities would be required to establish consistent practices for shipping, receiving, and storage of select agents and toxins to ensure that the entity has documented processes for securing and monitoring the shipment, receipt, and storage of these items.
- Entities would be required to supplement current training practices with security awareness and incident response training, as well as provide adequate training to inform individuals of the changes when a registered entity's security, incident response, or biosafety/biocontainment plans have been substantively altered.
- Entities would be required to maintain an accurate, current inventory of any animals or plants intentionally or accidentally exposed to or infected with a select agent (including number and species, location, and appropriate disposition).

Benefits and Costs

The APHIS and CDC proposed rules would update the regulations on select agents and toxins as contained in 7 CFR Part 331, 9 CFR Part 121, and 42 CFR Part 73. These regulations require registration, biocontainment/biosafety, incident response, and security measures for the

possession, use, and transfer of the listed select agents and toxins. The regulations are intended to prevent the misuse of those select agents and toxins, and therefore reduce the potential for those pathogens to harm humans, animals, animal products, plants or plant products in the United States. The proposed changes to the regulations would provide certain benefits associated with the added measures, as well as certain compliance costs for affected entities. Benefits and costs associated with the proposed regulations are outlined in this section.

Entities Affected by Reorganization of Select Agent and Toxin List

Entities that possess, use, or transfer HHS, VS, or overlap select agents or toxins would be affected by the Tier 1 classification of this rule. The affected entities include research and diagnostic facilities, Federal and State governmental entities, academic institutions, and commercial and non-profit institutions. Currently, there are 376 entities registered with APHIS and CDC. Of these active registered entities, there are 290 registered to possess the proposed Tier 1 select agents and toxins, including 87 academic, 34 commercial, 106 State government, 47 Federal government, and 16 private (non-profit) institutions.[11] Moreover, there are 13,630 individuals across all 376 entities registered with APHIS and CDC with an approved security risk assessment (SRA). The Tier 1 select agent and toxin assignment by agency is listed in the table below.

[11] It should be noted that the areas housing select agents and toxins of these affected entities tend to be small, with an estimated 500 to 2000 square feet and fewer than 10 individuals with access to the agents and/or toxins. Small laboratories within a larger facility are the rule, and dedicated buildings are the exception. As such, the costs of complying with additional security measures are expected to be minimal, given the relatively small physical space housing the select agents and toxins .

Table 1. Numbers of entities expected to be affected by proposed Tier 1 select agent and toxin classifications

Tier 1 Select Agent and Toxin Assignment					
Agency	**Academic**	**Commercial (Profit)**	**State Government**	**Federal Government**	**Private (non-Profit)**
APHIS	7	6	3	2	0
CDC	80	28	103	45	16
Total	87	34	106	47	16

Benefits

The proposed rule would create a means of ensuring improved oversight of the transfer, storage, and use of select agents and toxins; define the security procedures and background checks for pre-access suitability and continual monitoring of individuals with access to Tier 1 agents; and require that entities in possession of such agents develop and implement effective means of biosafety, information security and physical security. The overall benefit of these provisions is a reduced likelihood of accidental and intentional releases of select agents and toxins and the consequent avoidance of costs associated with such a release.

Protecting U.S. Agriculture

Should any select agent or toxin be intentionally introduced into the United States, the consequences would be significant. Direct losses in agriculture could occur as a result of the exposure, such as death or debility of affected animals or yield losses in crop production. Industry could also be affected through the imposition of domestic and foreign quarantines that result in a loss of markets. The Federal and State governments would also incur costs associated with eradication and quarantine enforcement to prevent further spread and – in the case of intentional introduction – law enforcement. In addition, there is the potential for a disruption or shortage in the domestic food supply, whether through contamination, consumer perception, or both. Past food safety incidents have shown that consumer perceptions (both domestic and

international) about an implicated food product and the producing country or sector's ability to produce safe food are slow to recover and can have a lasting influence on food demand and global trade.[12] The benefits of the proposed rule are the avoided losses of animals or plants that could be attacked by these organisms or toxic materials (because of the reduced risk of release of the select agents and reduced likelihood of exposure for susceptible animals or plants), the avoided public and private costs of eradication, and the avoided negative effects on products and markets.

The costs associated with the outbreak of a select agent can be very high, as demonstrated, for example, by the losses to agriculture and the food chain from the foot-and-mouth disease (FMD) outbreak in the United Kingdom in 2001. Those costs amounted to about £3.1 billion ($4.7 billion).[13] In 1999, it was estimated that the potential impacts of an FMD outbreak in California alone would be between $8.5 billion and $13.5 billion.[14] Another study estimated that the value of U.S. exports would decline by as much as 13 percent due in part to the decline in livestock supply, the anticipated embargo on susceptible U.S. exports, and consumer fears regarding FMD.[15]

Rinderpest is a contagious viral disease of cattle, buffalo, and some wild species of cloven-hoofed animals, such as giraffe and wildebeest, which can cause 100 percent illness if susceptible animals come in contact with infected animals or contaminated surfaces. As the result of an extensive international campaign consisting of vaccinations, clinical disease

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[12] Buzby, J.C. *Effects of food-safety perceptions on food demand and global trade*. Changing Structure of Global Food Consumption and Trade /WRS-01-1. Economic Research Service/USDA.
[13] Thompson, D., P. Muriel, D. Russell, P. Osborne, A. Bromley, M. Rowland, S. Creigh-Tyte, and C. Brown. *Economic costs of the foot and mouth disease outbreak in the United Kingdom in 2001*. Rev. Sci. Tech. 21,675–687, 2002.
[14] Ekboir, J.M. *Potential impact of foot-and-mouth disease in California: the role and contribution of animal health surveillance and monitoring services*. Davis, CA: Agricultural Issues Center, Division of Agriculture and Natural Resources, University of California, Davis, 1999.
[15] Paarlberg, P.L., J.G. Lee, A.H. Seitzinger. *Potential revenue impact of an outbreak of foot-and-mouth disease in the United States.* Vet Med Today: Food Animal Economics, JAVMA, Vol 220, No. 7, 2002.

research, serological surveillance sampling, contingency planning, and laboratory support in affected regions, rinderpest has been eradicated globally this year. Should Rinderpest be released into the environment once again, a serious outbreak would endanger livestock and susceptible wildlife. One conservative estimate of the cost of control and animal health alone in Asia and Africa since 1986 was estimated at $610 million.[16] Losses associated with herd fatalities and the effects on trade would likely be more than double this cost.

Protecting Public Health and Safety

Each of the agents placed on the HHS select list poses a severe threat to public health and safety. The benefits of the proposed rule result from the strengthened prevention against either accidental or intentional release of a biological agent or toxin. The cost of such an event in human life could be very high. An outbreak of one of the select biological agents or toxins would require a complex and expensive emergency response effort. This effort could include extensive public health measures, such as quarantine, isolation, preventative treatment and health testing for large numbers of potentially exposed persons, and extensive decontamination. Substantial costs could be incurred by hospitals and other medical facilities and institutions of government at all levels.

An outbreak, or widespread fear of one, also would likely create significant secondary effects to society including a potentially rapid increase in health anxiety among healthy individuals. This would likely result in overcrowded healthcare facilities and emergency rooms, the disruption of everyday business operations, the disruption of transportation, and many other aspects of normal behavior on both a short-term and long-term basis.

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[16] Normile, D. *Rinderpest. Driven to extinction*. Science, Vol 319, No. 5870, 2008.

Impacts from the October 2001 anthrax attacks exemplify the costs that the proposed regulatory revisions would help to prevent. The anthrax attacks caused 5 fatalities and 17 illnesses, disrupted business and government activities, closed substantial parts of the Postal Service, and caused widespread apprehension and changes in behavior. Costs included more than $23 million to decontaminate one Senate office building, approximately $2 billion in revenues lost to the postal service, and as much as $3 billion in additional costs to the Postal Service for cleanup of contamination and procurement of mail-sanitizing equipment.[17] Substantial costs due to lost productivity throughout the economy and from ongoing costs of the investigations into the incident are additional impacts.

An outbreak of smallpox, which was eradicated globally in 1979, would have a huge negative impact on human health and economic stability. Based on an analysis performed by the Department of Homeland Security, it is estimated that the U.S. economic losses associated with an intentional smallpox virus release could exceed $70 billion, including costs associated with public avoidance and tourism losses. Human health consequences (fatalities and illnesses) would be significant. The human health consequences associated with such a release include onward transmission of disease. Even if limited to a single (target) city, the economic losses represent losses to the entire nation. Direct costs of the release would include decontamination and site remediation costs, medical treatment costs, business disruption, and lost economic productivity due to fatalities in the city of the release. Additionally, direct costs associated with decreases in international tourism and public avoidance due to fear of further releases and exposure to contagion is assumed to affect the entire U.S. economy. These direct impacts would

[17] "Regulatory Impact Analysis for 42 CFR Part 73: Possession, Use, and Transfer of Select Biological Agents and Toxins Final Rule. Centers for Disease Control and Prevention, Department of Health and Human Services. February 3, 2005."
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"The US Postal Service Response to the Threat of Bioterrorism through the Mail, " Congressional Research Service Report for Congress, February 2002. <http://www.au.af.mil/au/awc/awcgate/crs/rl31280.pdf.> Date Accessed: May 18, 2010.

cause a ripple effect throughout the national economy as changes in demand and consumption affect related industries and households that may not experience any of the initial consequences.

These are examples of the exceedingly costly consequences of disease introduction into society. Deliberate introduction greatly increases the probability of a select agent or toxin becoming established and causing wide-ranging and devastating impacts on an economy, loss of market access for consumer goods and services, disruption to society, and diminished confidence in public and private institutions.

Costs

The entities affected by the proposed rule include research and diagnostic facilities, Federal, State and university laboratories, and private commercial and non-profit enterprises. An entity that possesses, uses, or transfers listed select agents or toxins is required to comply with the select agent regulations. The regulations require registering the possession, use, and transfer of select agents or toxins. In addition, the entity is also required to ensure that the facility where the agent or toxin is housed has adequate biosafety and containment measures, that the physical security of the premises is adequate, that all individuals with access to select agents or toxins have the appropriate education, training and/or experience to handle such agents or toxins, and that complete records concerning activities related to the select agents or toxins are maintained.

The proposed rule is intended to further ensure prevention of misuse of select agents and toxins that have the potential to pose a severe threat to both human and animal health, to plant health, or to animal and plant products. APHIS and CDC recognize that several of the required measures of the proposed regulations would undoubtedly impose certain operational costs upon affected entities, particularly to those entities with the newly classified Tier 1 select agents and toxins. The affected entities vary widely, and, as such, the proposed changes would have varying impacts. In some cases, the affected entities may already employ the required measures

or possess the resources necessary to meet these operational requirements. In other cases, the affected entities would be required to make budgetary allotments to meet the regulatory requirements. Information on specific changes at any individual site and, thus, those costs are not readily available. However, some general observations regarding the potential costs can be made. These costs are shown in table 2 at the end of this section.

Requirements of Responsible Official

The designated responsible official is an employee of a facility in charge of ensuring compliance with the select agent regulations. Among the duties of the responsible official, he or she must be familiar with the regulations contained in 7 CFR Part 331, 9 CFR Part 121, and 42 CFR Part 73 (as appropriate), and must have authority and responsibility to act on behalf of the entity. The proposed changes to the regulations would require that the designated responsible official, as well as any alternate responsible official, possess the appropriate training or expertise necessary to execute their required duties. In many cases, the currently designated responsible official and alternate responsible official are trained professionals in handling select agents and toxins. The incremental costs of the proposed rule associated with the requirements of the responsible official, as well as any alternate(s), would be those costs incurred to fill any knowledge gaps regarding the oversight of select agents and toxins, which could involve coursework/training/travel costs. The rule would clarify that the responsible official would also be the designee for maintaining training records, as the current regulations require such recordkeeping but provide no further specification. We estimate an annual time cost associated with the additional recordkeeping duties of approximately 29 hours per entity. We estimate that all registered entities would devote a total of 10,947hours annually to the recordkeeping provisions of the proposed regulations.

New Requirements for Conducting a Security Risk Assessment

Under the proposed changes to the regulations, individuals would be required to undergo a security risk assessment every 3 years as opposed to the current standard of every 5 years. This change would allow for the more timely identification of individuals whose status has fallen into one of the prohibited or restricted categories. With an estimated cost of $240 per person for providing background checks, incurred by the Federal Bureau of Investigation's Criminal Justice Information Services (FBI/CJIS), the proposed measure would increase the frequency of FBI/CJIS security risk assessments by approximately 67 percent. However, the benefit in terms of reduced risk of being able to identify individuals whose status has fallen into one of the prohibited or restricted categories within 3 rather than 5 years would outweigh the increase in cost. The annual estimated cost to FBI/CJIS would increase to approximately $1.16 million from an annual cost of $719,388 every 5 years for all 13,630 approved SRAs.[18] The increased cost of this provision of conducting security risk assessments for all 13,630 approved SRAs would be approximately $442,644 (or 62 percent) annually.

Revisions to Security, Biocontainment/Biosafety, and Incident Response Plans

Entities would be required to revise and implement security, biocontainment/biosafety, and incident response plans to include provisions to address the safeguarding of animals or plants intentionally or accidentally exposed to or infected with select agents. These proposed revisions to each plan are intended to be a comprehensive reflection of the regulations and provide necessary guidance regarding the handling of animals and plants inoculated with select agents.

[18] Annual cost is defined as ———. Annual costs are based on a current interest rate of 3.25 percent as reported as the current bank prime loan interest rate reported by the Board of Governors of the Federal Reserve System, August 24, 2011.

Security Plan

According to the proposed changes to the regulations, the security plan would be submitted for initial registration and renewals of registration, in addition to the current standard of submission upon request. The affected entities would incur an additional cost related to shipment of the security plan to the agency, unless submitted via electronic mail or fax. A Postal Service Mail Flat Rate envelope would cost $4.95 to mail. We estimate an average of 130 entities would be renewing their registration with the Select Agent Program per year. If these entities chose to submit their security plans via the mail, it would cost $643.

The proposed regulations add provisions for information security into the security plan. These measures include network connectivity monitoring, restriction of user permissions to only mission-specific files and applications, measures to prevent network infiltration by malicious code, and configuration management including regular patching and system software updates. These measures are consistent with industry recommendations on information security policy. Inappropriate access by unauthorized personnel, internal and external misuse of resources, and the threat of malicious code can impact the integrity of the research conducted at facilities, as well as threaten the containment of select agents and toxins. According to a recent study, malicious attacks alone are on the rise with an increase in such attacks from 12 percent of breaches in 2008 to 24 percent of breaches in 2009.[19] The cost of implementing these information security measures would vary among the affected entities based upon current level of information security at each facility. The specific requirements of the proposed changes to information security that must be outlined in an entity's security plan include:

[19] "2009 Annual Study: US Cost of Data Breach," Ponemon Institute Research Report, January, 2010. <http://www.ponemon.org/local/upload/fckjail/generalcontent/18/file/US_Ponemon_CODB_09_012209_sec.pdf> Date Accessed: May 18, 2010.

- Means to ensure that all external connections to the systems which control security of the facility are isolated or have controls that permit and monitor for only authorized and authenticated user access. The estimated cost of firewall software ranges between $24 and $37 per license or between $9,024 and $13,912 for each license across all 376 registered entities. Encryption software is estimated to cost between $79 and $199 per system or between $29,704 and $74,824 for each system across all 376 registered entities;
- Means to ensure only authorized and authenticated users have access to information, files, and equipment needed to fulfill their roles and responsibilities, and access is amended as their roles change. Based on site-specific inspections, we believe the affected entities already employ the required measures;
- Means of preventing malicious code from impacting critical information systems. The cost for antivirus software is estimated at $80 per user per year or up to $1,090,400 per user per year for all 13,630 approved SRAs. Computer intrusion detection software is estimated at $15 per computer or approximately $5,640 for each computer across all 376 registered entities;
- Means for a robust configuration management practice for information systems to include regular patching and updates made to operating systems and individual applications. Such activity would require the time of the computer system administrator. It is estimated this could take up to 8 hours per month at $25 per hour for a total of $200 per month per entity or up to $902,400 per year for all 376 registered entities; and

- Implement backup security measures in the event that access control systems and/or surveillance devices are rendered inoperable. The use of security guards, for example, to ensure safekeeping of select agents and toxins under such circumstances is estimated at approximately $8 to $25 per hour or $3,008 to $9,400 per hour across all 376 registered entities, depending on location.[20]

The security plan would also require entities to establish consistent practices for shipping, receiving, and storage of select agents and toxins to ensure that the entity has documented processes for securing and monitoring the shipment, receipt, and storage of these items. This requirement is designed to clarify current language in the regulations, and would cost little more than the time it takes to revise the security plan.

In addition to the preceding description of proposed changes to the security plan for affected entities, the security plan for an entity possessing a Tier 1 select agent or toxin must also include relevant security measures that may result in additional costs of operation.

The security plan must describe procedures for, as outlined in the proposed regulations, individuals who would have access to a Tier 1 select agent or toxin. These procedures must include reporting of incidents or conditions that could affect an individual's ability to safely work with select agents and toxins or to safeguard them from theft, loss or release. These procedures must also include the training of all entity employees on entity policies and procedures for reporting, evaluation, and corrective actions concerning the assessment of personnel suitability to access Tier 1 agents and toxins. Finally, the security plan must describe procedures for how an entity's responsible official would coordinate their efforts with the

[20] This proposed revision would affect those entities relying solely on information systems for security. We do not anticipate a significant increase in costs to registered entities as a result of this provision as most entities already employ non-security security measures in addition to information security.

entity's safety and security professionals to ensure security of Tier 1 select agents and toxins and share, as appropriate, relevant information. In addition to the time cost associated with revising the security plan to account for these Tier 1 modifications, it is estimated that the cost for conducting a pre-access suitability assessment of personnel would likely include identity verification, credential/education verification, and a police background check. The cost of performing these tasks could range between $100 and $120 per SRA approved individual working with Tier 1 agents, and would likely reach approximately $1.4 and $1.6 million if all 13,630 approved SRAs had access to Tier 1 select agents.[21]

Entities with Tier 1 select agents and toxins would be required to have a minimum of three barriers where each subsequent barrier is different and adds to the delay in reaching secured areas where select agents and toxins are used or stored. Based on information received through site-specific inspections, it is estimated that the affected entities currently implement, at least, the minimum barriers. Therefore, this requirement is also designed to clarify current language in the regulations, and would likely cost the time it takes to revise the security plan. All registered space or areas that reasonably afford access to the registered space with Tier 1 select agents and toxins must be protected by an intrusion detection system (IDS) unless physically occupied, and must be staffed with personnel monitoring the IDS who are capable of evaluating and interpreting the alarm and alerting the designated security response force or law enforcement. Entities possessing Tier 1 select agents and toxins must also provide backup power and energy sources to power information security networks and integrated access controls and related systems during emergencies. For facilities with electronic security networks, a generator for a building could cost as much as $40,000. A back-up home generator for a smaller lab space

[21] We note that not all SRA approved individuals work with Tier 1 agents, and estimated cost is likely overstated.

could run between $300 and $6,000. Again, based on information received through site-specific inspections, it is generally believed that the affected entities already employ backup power and energy sources as such practices are a generally recognized industry standard.

Entities would be required to conduct complete inventory audits of all Tier 1 select agents and toxins in long-term storage upon the physical relocation of a collection or inventory of select agents or toxins, upon the departure or arrival of a principal investigator for those Tier 1 select agents or toxins, or in the event of a theft or loss of a Tier 1 select agent or toxin. There is an associated time cost to conduct an inventory check, especially when there must be a procedure in place to protect the integrity of the research associated with the inventory. We invite public comment on the costs associated with the specifics of this provision to conduct complete inventory audits of all Tier 1 select agents and toxins.

The proposed changes to the regulations would impose further measures to ensure security on entities that possess foot-and-mouth disease virus and rinderpest virus. These entities would be required to have a minimum of four barriers, one of which must be a perimeter security fence or equivalent which is monitored 24 hours a day and 7 days a week to detect the presence of unauthorized persons, vehicles, materials, or unauthorized activities. These facilities must further provide an on-site armed security response force with a roving patrol 24 hours a day and 7 days a week. Response time must not exceed 5 minutes from the time of an intrusion alarm or report of a security incident. Additionally, facilities possessing foot-and-mouth disease virus and rinderpest virus must provide CCTV surveillance with monitoring and recording 24 hours a day and 7 days a week, and a transport vehicle with GPS tracking designed to serve as a containment vehicle. The proposed changes to the regulations would impose further measures to ensure security on entities that possess Variola major or Variola minor virus. These entities must require

personnel with access to Variola major or Variola minor virus to have a Top Secret security clearance, require Variola major or Variola minor virus storage locations be under the surveillance of closed circuit television that is monitored, and limit after-hours access to Variola major or Variola minor virus only to individuals with specific permission from the principal investigator responsible for the Variola major or Variola minor virus. After-hours access procedures must require notification of the entity's security staff prior to entry into the Variola laboratory and upon exit. These facilities must further require that observation zones be maintained in outdoor areas adjacent to the physical barrier at the perimeter of the entity and be large enough to permit observation of the activities of people at that barrier in the event of its penetration, provide for a minimum of four barriers for the protection of the Variola major or Variola minor virus, one of which must be a perimeter fence, require a numbered picture badge identification subsystem to be used for all individuals who are authorized to access Variola major or Variola minor without escort, require the use, at all times, of properly trained, and equipped security force personnel able to interdict threats identified in the site specific risk assessment, identify security force personnel designated to strengthen onsite response capabilities, and who would be onsite and available at all times to carry out their assigned response duties, provide for security patrols to periodically check external areas of the registered areas to include physical barriers and building entrances, require that all on-duty security force personnel shall be capable of maintaining continuous communication with support and response assets by way of security operations center, require that Variola major and Variola minor material in long term storage be stored in tamper-indicating containers, require that all spaces containing working or permanent Variola major or Variola minor stocks be locked and protected by an intrusion alarm system that is activated upon the unauthorized entry of a person anywhere into the area, require that alarms

required pursuant to this section annunciate in a continuously manned security operations center located within the facility, and require that the security operations center shall be located within a building so that the interior and is not visible from the perimeter of the protected area.

APHIS and CDC believe all affected entities are currently in compliance with these added measures based on information obtained through site-specific inspections.

Biocontainment/Biosafety and Incident Response Plans

According to the proposed changes to the regulations, the biocontainment/biosafety and incident response plans would require enhanced detail of operational procedures. Specifically, the biocontainment/biosafety plan would describe biosafety and containment procedures for animals or plants intentionally or accidentally exposed to or infected with a select agent. The incident response plan would be based on a site-specific risk assessment. The response procedures in the incident response plan must account for hazards associated with the select agent or toxin and appropriate actions to contain such select agent or toxin, including any animals or plants intentionally or accidentally exposed to or infected with a select agent. The incident response plan would also include policies or procedures for entities with Tier 1 select agents or toxins. These include the entity's response procedures for failure of intrusion detection or alarm system, and notification procedures for the FBI in the event of a theft or suspicious activity that may be criminal in nature involving a Tier 1 select agent or toxin.

These proposed changes to the regulations would enhance the effectiveness of these plans. As the proposed changes are related to the actual documentation of the biocontainment/biosafety and incidence response plans, we do not anticipate that such changes would impose costs to affected entities outside of the additional time required to include these measures.

Additionally, the biocontainment/biosafety plan would include an occupational health program, along with required enrollment, for individuals with access to Tier 1 select agents and toxins. Occupational health programs may include baseline assessments (e.g., physical exam, vaccinations, diagnostic laboratory testing, blood tests, and general healthcare screening) and regular physical examinations. The cost of an appropriate, cost effective occupational health program is dependent on various factors including location, number of SRA approved individuals working with Tier 1 select agents, and the bundle of services offered. We estimate the cost of a comprehensive occupational health care program to establish baseline assessments would range between $107 and $204 per SRA approved individual working with Tier 1 agents. We further estimate that the implementation of a comprehensive occupational health care program would cost between $1.5 million and $2.8 million should all 13,630 approved SRAs participate.[22] Since we understand that there may be additional costs to implement an occupational health program where none is currently available to SRA approved individuals working with Tier 1 agents, we invite public comments on these costs to establish an occupational health program.

Training

The proposed regulations would require entities to supplement current training practices with security awareness and incident response training. Furthermore, entities would be required to provide training if a registered entity's security, incident response, biosafety or biocontainment plans is substantively altered. Entities with Tier 1 select agents and toxins must conduct annual insider threat awareness briefings on how to identify and report suspicious

[22] We again note that not all SRA approved individuals work with Tier 1 agents, and this estimated cost is likely overstated.

behaviors. The cost of supplemental training would be a time cost added to the training programs currently required.

Table 2. Summary of the expected required costs of the proposed rule[1]

	Entity Cost	***Units***	***Total Cost***
Added Costs to Government			
Increased frequency of FBI/CJIS background checks	$240 per person	13,630 approved SRAs	$442,644 annually[2]
Total Added Cost to Government	**$442,644 annually**		
Added Costs to Affected Entities			
Security Plan			
Submission of Plan	$4.95 per submission	Estimated 130 annual renewals plus 5 pending	$643.50
Information Security[3]			
network connectivity monitoring (encryption software)	$24-37 per license	376 registered entities	$9,024 – 13,912
network connectivity monitoring (firewall software)	$79 - 199 per system	376 registered entities	$29,704 – 74,824
malware software (antivirus)	$80 per user per year	13,630 approved SRAs	$1,090,400 per year
malware software[3] (intrusion detection)	$15 per computer	376 registered entities	$5,640
system software updates (dedicated time for IT Specialist)	$2,400 per year	376 registered entities	$902,400 per year
Total Costs Across All Affected Entities	**$2.04 – 2.09 million**		
Added Costs of Tier 1 Status[4]			
Pre-suitability Assessment[5]	$100 - 120 per person	13,630 approved SRAs	$1.36 – 1.64 million
Occupational Health[5] Program	$107 – 204 per person	13,630 approved SRAs	$1.46 – 2.78 million
Total Added Costs of Tier 1 Status	**$2.82 – 4.42 million**		
Total Costs to Government and Across All Affected Entities[6]	**$5.30 – 6.95 million**		

[1] The costs summarized in this table are actual expenditures expected to be incurred. In addition, there would be the opportunity cost of additional time required to comply with proposed measures. Time costs are noted qualitatively in the Benefits and Costs section of this analysis.
[2] Please see footnote 18 of this document.
[3] We emphasize that total estimated costs across all entities are uncertain as complete information is unavailable regarding total number of computers per affected entity.
[4] We emphasize that, based on site specific inspections, many of the entities currently have similar provisions in place.
[5] We emphasize that the estimated costs are likely overstated as not all SRA approved individuals have access to Tier 1 agents. This calculation assumes a single computer is used for covered work.
[6] We emphasize that total estimated costs across all entities are overstated where incomplete information is available.

Recordkeeping

Entities would be required to maintain an accurate, current inventory of any animals or plants intentionally or accidentally exposed to or infected with a select agent (including number and species, location, and appropriate disposition). We understand that there may be additional costs associated with maintaining an accurate, current inventory of any animals or plants intentionally or accidentally exposed to or infected with a select agent (including number and species, location, and appropriate disposition) other than those costs associated with the time spent on maintaining the inventory. We invite public comments on any additional costs that may be incurred to be in compliance with this proposed provision.

Initial Regulatory Flexibility Analysis

The Regulatory Flexibility Act requires agencies to evaluate the potential effects of their proposed and final rules on small businesses, small organizations and small governmental jurisdictions. Section 603 of the Act requires agencies to prepare and make available for public comment an initial regulatory flexibility analysis that describes expected impacts of a proposed rule on small entities.

Reasons Action is Being Considered

Section 201 of Subtitle A and Section 212(a) of Subtitle B[23] of the *Public Health Security and Bioterrorism Preparedness and Response Act of 2002* (Pub. L. 107-188) (the Act), requires the Secretaries of Health and Human Services and Agriculture, respectively, to establish and maintain a list of each biological agent and each toxin that they have determined to have the potential to pose a severe threat to human, animal or plant health, or to animal or plant products. Each respective Secretary is further required to review and republish the select agent list

[23] Title II (Enhancing Controls on Dangerous Biological Agents and Toxins)—Subtitle B (Department of Agriculture) of Public Law 107-188 may be cited as the "Agricultural Bioterrorism Protection Act of 2002."

biennially or more often as needed and revise the list as necessary. Each respective Secretary implements regulations which include the provisions of the Act, and set forth the requirements for possession, use and transfer of select agents and toxins. Revision of these regulations is in compliance with the policy outlined in Executive Order 13546, "Optimizing the Security of Biological Select Agents and Toxins in the United States." The Executive Order requires that the Secretaries of Health and Human Services and Agriculture publish proposed regulations to establish risk based tiering of the select agent list, and revise the regulations, rules, and guidance to accommodate a tiered select agent list no later than October 2011.

This proposed rulemaking provides the public with notice of the revisions and the opportunity to review and provide comment.

Objectives of and Legal Basis for the Rule

The Act provides for the regulation of biological agents and toxins that have the potential to pose a severe threat to both human and animal health, to plant health, or to animal and plant products. The criteria for determining whether to include an agent or toxin on the list are outlined in the Act. The Animal and Plant Health Inspection Service (APHIS) has the primary responsibility for implementing the provisions of the Act within the Department of Agriculture (USDA), and the Centers for Disease Control and Prevention (CDC) has the primary responsibility for implementing the provisions of the Act within the Department of Health and Human Services (HHS).

The Act requires a biennial review and republication of the select biological agent and toxin list, with revisions as appropriate in accordance with this law. The action would implement the revision and republication of the list following the recommendations of the third biennial review of the list. Revision of these regulations is also required for compliance with the policy outlined in Executive Order 13546, "Optimizing the Security of Biological Select Agents

and Toxins in the United States," which requires the Secretaries of Health and Human Services and Agriculture to publish proposed regulations to establish risk based tiering of the select agent list, and revise the regulations, rules, and guidance to accommodate a tiered select agent list no later than October 2011.

Potentially Affected Small Entities

The entities most likely to be affected by this rule are those laboratories and other institutions conducting research and related activities entities in possession of Tier 1 select agents or toxins, and, to a somewhat lesser extent, those entities possessing the newly added select agents and toxins. Affected entities (other than Federal or State governmental entities) are most likely found within the following North American Industry Classification System 2007 (NAICS 2007) categories:

- 541711, 'Research and Development in Biotechnology';
- 541712, 'Research and Development in the Physical, Engineering, and Life Sciences (except Biotechnology);'
- 325412, 'Pharmaceutical Preparation Manufacturing;'
- 325413, 'In-Vitro Diagnostic Substance Manufacturing;'
- 325414, 'Biological Product (except Diagnostic) Manufacturing;'
- 541940, 'Veterinary Services;'
- 611310, 'Colleges, Universities and Professional Schools;'
- 621511, 'Medical Laboratories;'
- 622110, 'General Medical and Surgical Hospitals.'

The Small Business Administration (SBA) has established guidelines for determining when entities are considered small. An entity classified within NAICS 541711, 541712, 325413 or 325414 is considered small with 500 or fewer employees, and one within NAICS 325412 is

considered small with 750 or fewer employees. An entity in NAICS 541940 or 611310 is considered small with annual receipts/revenues of $7 million or less. Entities classified within NAICS 621511 are considered to be small if they have annual receipts of not more than $13.5 million. An entity classified within NAICS 622110 are considered to be small with annual receipts of $34.5 million

While the breakdown of the size of the establishments, as reported by the 2007 Economic Census, does not precisely fit the SBA guidelines, the data indicate that the vast majority of the entities potentially affected by this rule, other than post-secondary institutions, can be considered small, as shown in table 3. According to the 2007 Economic Census, more than 98 percent of entities in NAICS 541711 and 541712, more than 92 percent of entities in NAICS 325412, more than 95 percent of entities in NAICS 325413, 96 percent of entities in NAICS 325414, 99 percent of entities in industry 541940, 89 percent of entities in industry NAICS 621511, and 35 percent of entities in industry 622110 can be classified as small entities.[24] According to data from the U.S. Department of Education's Integrated Postsecondary Education Data System (IPEDS), more than 14 percent of reporting post-secondary institutions had revenue of less than $7 million in fiscal year 2008-09, and could therefore be considered small.[25]

The majority of affected entities are likely to be small. Any entity that possesses, uses or transfers listed select agents or toxins is required to comply with the select agent regulations, and would likely incur costs associated with that compliance. Although the proposed regulations would likely result in additional costs for entities possessing Tier 1 select agents and toxins,

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[24] Based on the small business size standards matched to industries described in the North American Industry Classification System (NAICS), as modified by the Office of Management and Budget in 2007, and reported in the Small Business Administration's (SBA) Small Business Size regulations contained in 13 CFR 121.

[25] Source: United States Department of Education, Institute of Education Sciences, National Center for Education Statistics Integrated Postsecondary Education Data System (IPEDS).

these costs are small in comparison to the long-term benefits of protecting against the deliberate misuse of select agents and toxins that would result in devastating effects to the economy, such as the costs associated with potential outbreaks as discussed in the “Benefits and Costs” section of this document.

Table 3. Prevalence of small entities within industries expected to be directly affected by the proposed rule.

NAICS Code	Number of Firms		Total Revenue, Receipts, or Value of Shipments	
SBA Small-entity Standard based on Employment	< 500 Employees	500 + Employees	< 500 Employees	500 + Employees
541711 R&D in Biotechnology (commercial and non-profit)	1,954	35	$8.8b	$8.4b
541712 R&D in the Life Sciences (commercial and non-profit)	7,696	135	$27.2b	$43.9b
325412 Pharmaceutical Preparation mfg [a/]	916	75	$55.8b	$87.0b
325413 In-vitro Diagnostic Substance Mfg[a/]	245	14	$6.3b	$4.1b[b/]
325414 Biological Product (except Diagnostic) Mfg [a/]	335	15	$6.9b[b/]	$9.5b[b/]
SBA Small-entity Standard based on Annual Receipts	< $10 million in Receipts	$10 million + in Receipts	< $10 million in Receipts	$10 million + in Receipts
541940 Veterinary Services	24,422	53	$21.4b	$587m
621511 Medical Laboratories	2,186	258	$3.7b	$19.0b
622110 General Medical and Surgical Hospitals	1,067	1,984	$12.7b[b/]	$644.4b
611310 Colleges, Universities, and Professional Schools	Employment breakdown Undetermined		Receipts Undetermined	

[a] The size standard is measured by the number of establishments for this NAICS series rather than by the number of firms since the Economic Census does not provide statistics on the breakdown on size by the number of firms. As a result, the proportion of small entities may be inflated.
[b] Figure excludes proprietary data.
Source: The 2007 Economic Census. Department of Commerce, Census Bureau.

Projected Reporting, Recordkeeping, and Other Compliance Requirements

Reporting and recordkeeping requirements associated with the proposed rule are discussed in the "Benefits and Costs" section of this document and in proposed rules APHIS-2009-0070 and CDC-2011-0012 under the heading "Paperwork Reduction Act."

Duplication, Overlap, or Conflict with Existing Rules and Regulations

APHIS and CDC are working in a joint effort to ensure that any duplication, overlap, or conflicts of this proposed rule with other Federal rules are minimized. As such, APHIS and CDC are proposing parallel changes to their overlap select agent regulations.

Alternatives to minimize Significant Economic Impacts of the Rule

Implementation of this rule would be in accordance with the *Public Health Security and Bioterrorism Preparedness and Response Act of 2002*. We considered two alternatives to the chosen course of action. One alternative would be to maintain the status quo and rely on the current regulations found in 7 CFR Part 331, 9 CFR Part 121, and 42 CFR Part 73. We rejected this option because it would not fulfill the implementation responsibilities of the Departments of Agriculture and Health and Human Services. The Act requires the Secretaries to review and republish the list of select agents and toxins every 2 years and to revise the list as necessary.

Revision of these regulations is in compliance with the policy outlined in Executive Order 13546, "Optimizing the Security of Biological Select Agents and Toxins in the United States." The Executive Order requires that the Secretaries of Health and Human Services and Agriculture publish proposed regulations to establish risk-based tiering of the select agent list, and revise the regulations, rules, and guidance to accommodate a tiered select agent list no later than October 2011. Maintaining the status quo would be a violation of the Act and the Executive Order.

Another alternative would be to lessen some of the requirements of the proposed rule that may pose a cost to affected entities. We also rejected this option. The proposed rule follows the recommendations provided in expert reports such as "The Report of the Workgroup on Strengthening the Biosecurity of the United States" and "Recommendations from the Federal Experts Security Advisory Panel." APHIS and CDC have determined that the additional costs associated with the proposed regulations would be small when compared to the reduction in risk of release of Tier 1 select agents and toxins into the environment.