

Report on the Potential Exposure to Anthrax

Centers for Disease Control and
Prevention

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Executive Summary

The Centers for Disease Control and Prevention (CDC) conducted an internal review of an incident that involved an unintentional release of potentially viable anthrax within its Roybal Campus, in Atlanta, Georgia. On June 5, 2014, a laboratory scientist in the Bioterrorism Rapid Response and Advanced Technology (BRRAT) laboratory prepared extracts from a panel of eight bacterial select agents, including *Bacillus anthracis* (*B. anthracis*), under biosafety level (BSL) 3 containment conditions. These samples were being prepared for analysis using matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry, a technology that can be used for rapid bacterial species identification.

What Happened

This protein extraction procedure was being evaluated as part of a preliminary assessment of whether MALDI-TOF mass spectrometry could provide a faster way to detect anthrax compared to conventional methods and could be utilized by emergency response laboratories. After chemical treatment for 10 minutes and extraction, the samples were checked for sterility by plating portions of them on bacterial growth media. When no growth was observed on sterility plates after 24 hours, the remaining samples, which had been held in the chemical solution for 24 hours, were moved to CDC BSL-2 laboratories. On June 13, 2014, a laboratory scientist in the BRRAT laboratory BSL-3 lab observed unexpected growth on the anthrax sterility plate. While the specimens plated on this plate had only been treated for 10 minutes as opposed to the 24 hours of treatment of specimens sent outside of the BSL-3 lab, this nonetheless indicated that the *B. anthracis* sample extract may not have been sterile when transferred to BSL-2 laboratories.

Why the Incident Happened

The overriding factor contributing to this incident was the lack of an approved, written study plan reviewed by senior staff or scientific leadership to ensure that the research design was appropriate and met all laboratory safety requirements. Several additional factors contributed to the incident:

- Use of unapproved sterilization techniques
- Transfer of material not confirmed to be inactive
- Use of pathogenic *B. anthracis* when non-pathogenic strains would have been appropriate for this experiment
- Inadequate knowledge of the peer-reviewed literature
- Lack of a standard operating procedure or process on inactivation and transfer to cover all procedures done with select agents in the BRRAT laboratory.

What Has CDC Done Since the Incident Occurred

CDC's initial response to the incident focused on ensuring that any potentially exposed staff were assessed and, if appropriate, provided preventive treatment to reduce the risk of illness if exposure had occurred. CDC also ceased operations of the BRRAT laboratory pending investigation, decontaminated potentially affected laboratory spaces, undertook research to refine understanding of potential exposures and optimize preventive treatment, and conducted a review of the event to identify key recommendations.

To evaluate potential risk, research studies were conducted at a CDC laboratory and at an external laboratory to evaluate the extent to which the chemical treatment used by the BRRAT laboratory inactivated *B. anthracis*. Two preparations were evaluated: vegetative cells and a high concentration of *B. anthracis* spores. Results indicated that this treatment was effective at inactivating vegetative cells of *B. anthracis* under the conditions tested. The treatment was also effective at inactivating a high percentage of, but not all *B. anthracis* spores from the concentrated spore preparation.

A moratorium is being put into effect on July 11, 2014, on any biological material leaving any CDC BSL-3 or BSL-4 laboratory in order to allow sufficient time to put adequate improvement measures in place.

What's Next

Since the incident, CDC has put in place multiple steps to reduce the risk of a similar event happening in the future. Key recommendations will address the root causes of this incident and provide redundant safeguards across the agency, these include:

- The BRRAT laboratory has been closed since June 16, 2014, and will remain closed as it relates to work with any select agent until certain specific actions are taken
- Appropriate personnel action will be taken with respect to individuals who contributed to or were in a position to prevent this incident
- Protocols for inactivation and transfer of virulent pathogens throughout CDC laboratories will be reviewed
- CDC will establish a CDC-wide single point of accountability for laboratory safety
- CDC will establish an external advisory committee to provide ongoing advice and direction for laboratory safety
- CDC response to future internal incidents will be improved by rapid establishment of an incident command structure
- Broader implications for the use of select agents, across the United States will be examined.

This was a serious event that should not have happened. Though it now appears that the risk to any individual was either non-existent or very small, the issues raised by this event are important.. CDC has concrete actions underway now to change processes that allowed this to happen, and we will do everything possible to prevent a future occurrence such as this in any CDC laboratory, and to apply the lessons learned to other laboratories across the United States.

Background

This report reviews circumstances leading to June 2014 incident in which CDC staff members were potentially exposed to viable *Bacillus anthracis*. The incident occurred after *B. anthracis* extract was transferred from CDC's Bioterrorism Rapid Response and Advanced Technology (BRRAT) biosafety level (BSL) 3 laboratory to BSL-2 laboratories without proper assurance that the extract did not contain viable cells or spores.

This is not the first time an event of this nature has occurred at CDC, nor the first time it occurred from the BRRAT laboratory. At the time of this writing, CDC is aware of four other such incidents in the past decade. In a prior incident in 2006, CDC's BRRAT laboratory transferred vials of anthrax DNA to two outside laboratories. The BRRAT laboratory believed that they had inactivated the samples, but upon receipt and testing of the samples, viable *B. anthracis* was detected. The BRRAT laboratory implemented new quality assurance procedures to ensure non-viability of DNA preparations of select agents and developed policies that require the signature of the laboratory's principal investigator prior to shipping or transferring DNA derived from bacterial select agents. These procedures were not followed in the current incident, which did not specifically involve preparation of DNA for transfer. Also in 2006, DNA preparations shipped from another CDC laboratory were found to contain live *Clostridium botulinum* due to the use of inadequate inactivation procedures. In 2009, newly available test methods showed that a strain of *Brucella*, thought to have been an attenuated vaccine strain and previously shipped to outside laboratories as early as 2001, was not the vaccine strain. The vaccine strain is not considered to be a select agent, while the strain that was actually shipped is a select agent.

As this report was being finalized, CDC leadership was made aware that earlier this year a culture of low-pathogenic avian influenza was unintentionally cross-contaminated at a CDC influenza laboratory with a highly pathogenic H5N1 strain of influenza and shipped to a BSL-3, select-agent laboratory operated by the United States Department of Agriculture (USDA). The CDC influenza laboratory where this incident occurred is now closed and will not reopen until adequate improvements are put in place. Although CDC is continuing to investigate and review this matter, Attachment A provides current information on the incident and the agency's response.

Effective, validated inactivation protocols for *B. anthracis* have been published. Cultures of *B. anthracis* cells and spores can be completely inactivated through established protocols using heat (e.g., boiling for 10 minutes or autoclaving for 15 minutes), irradiation (1 million rad), or various chemical treatments (e.g., hydrogen peroxide, peracetic acid, formalin, or gaseous ethylene oxide). In general, longer treatment times and/or higher concentrations are required for inactivation of spores compared to inactivation of viable cells. Solutions can also be sterilized by filtration, through a 0.1 micron filter, to remove viable cells and spores.

Space decontamination can be achieved through one of two approved liquid decontamination methods and one vapor method. A solution of freshly made dilution of household bleach (10% bleach by volume), pH adjusted to 7.0 with acetic acid, is recognized by the Environmental Protection Agency (EPA) to kill *B. anthracis* spores with a minimum contact time of 10 minutes. The EPA also registered the use of Spor-Klenz® (STERIS®) as a sterilant, as a 1:99 water dilution of the concentration is effective as a sporocide with a minimum contact time of 30 minutes. Vapor phase hydrogen peroxide is also available at CDC as a room disinfectant.

Laboratories

CDC laboratories conduct research that is critical to better detect, respond to, and prevent disease and bioterrorism. Research done in CDC laboratories helps identify better ways to detect these infectious agents rapidly. The Laboratory Response Network (LRN) is a network of laboratories that can respond to biological and chemical threats and other public health emergencies. It includes state and local public health, veterinary, military, and international labs. The BRRAT laboratory provides technical and scientific support for the approximately 150 laboratories in the LRN. The BRRAT laboratory contains both BSL-3 and BSL-2 labs and was established in 1999 in accordance with Presidential Decision Directive 39, which outlined national anti-terrorism policies and assigned specific missions to federal departments and agencies (<http://www.bt.cdc.gov/lrn/>). The BRRAT laboratory provides quality assurance for the specialized reagents used in the LRN and has performed studies with the goal of improving the performance and reliability of tests used to detect biological threat agents. *Bacillus anthracis* is of particular concern because it can and has been used as a weapon.

Two CDC laboratories received the extracts prepared by the BRATT laboratory BSL-3 laboratory: the Bacterial Special Pathogens Branch laboratory (BSPB laboratory); and the Biotechnology Core Facility Branch (BCFB laboratory).

Methods Used in Reviewing this Incident

A CDC team of scientists and leaders interviewed laboratory scientists involved directly with the incident and others who had specific knowledge of the incident and of immediate response activities. Each interview consisted of a standardized set of questions, as well as specific questions based on an individual's role and responsibilities. Standard operating procedures (SOPs), protocols, and training records were also reviewed.

Description of the Event

Appendices B and C provide a timeline of major events.

The BRRAT laboratory was evaluating matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry, which can identify bacteria by bacterial protein “fingerprints.” It is faster and less expensive than conventional species-identification methods, which require culture of organisms on selective bacterial media or extraction and characterization of bacterial nucleic acids. The project was a collaboration among the BRRAT, BSPB, and BCFB laboratories. The researchers intended to use the data collected to submit a joint proposal to CDC’s Office of Public Health Preparedness and Response to fund further evaluation of the MALDI-TOF method because MALDI-TOF is increasingly being used by clinical and hospital laboratories for infectious disease diagnostics.

On June 2, 2014, the BRRAT laboratory supervisor contacted a subject matter expert who had successfully used this technology to identify three pathogenic species of *Brucella*. In response to the BRRAT laboratory supervisor’s request for assistance and advice, a BSPB laboratory supervisor offered to share the methodology, results, and inactivated bacterial preparations used by the BSPB laboratory in their work with *Brucella*. The BSPB laboratory had modified the MALDI-TOF equipment manufacturer’s sample preparation protocol to optimize the results for bacterial protein sample extractions of *Brucella*. In this extraction procedure, each organism is treated with ethanol, then with 70% formic acid for 10 minutes, followed by the addition of 100% acetonitrile, and then is incubated at room temperature. The method used by the BSPB laboratory also incorporated a sterility check of the extract after 10 minutes of incubation in the extraction solution. Specifically, an aliquot of the extract was spread on an agar plate, incubated for 48 hours, and then examined for growth. If no growth was visible, the extract was considered to be sterile and could be safely transferred from the BSL-3 laboratory to a BSL-2 laboratory for processing for use in the MALDI-TOF equipment.

The BSPB laboratory protocol did not call for filtration of the bacterial extract prior to transfer from the BSL-3 laboratory because it had been determined that the extraction procedure inactivated the three species of *Brucella* tested. It is important to note that, unlike *B. anthracis*, *Brucella* does not form spores. Bacterial spores are relatively resistant to harsh conditions, such as the chemicals used in this extraction procedure, and are more difficult to kill than vegetative cells. As a result, additional procedures (e.g., filtration) can be used when working with spore-forming bacteria, such as *B. anthracis*, to ensure specimens are rendered non-viable.

The BRRAT laboratory supervisor instructed a laboratory scientist to obtain the written protocol for sample preparation from BSPB laboratory. The BSPB laboratory provided a sample preparation protocol, which did not include a viability SOP. The supervisor requested that virulent strains of eight select agents, including *B. anthracis*, be used for the initial experiment. On June 5, 2014, the laboratory scientist followed the modified protocol to prepare eight individual organism extracts for use in the MALDI-TOF. Another scientist in the BRRAT laboratory raised the question of whether filtration of the extracts might affect the MALDI-TOF results. To answer this question the laboratory scientist split each extract into two aliquots and filtered one aliquot through a 0.1 micron filter. After a 10 minute incubation period, filtered and unfiltered extracts were then plated onto agar and incubated for 24 hours to check the extracts for sterility. The decision to incubate for 24 hours, rather than 48 hours (as recommended by the BSPB staff member) was made by the first laboratory scientist based on the

individual's own understanding of information conveyed by the laboratory scientist in the BSPB laboratory during a telephone discussion of the protocol.

All work was performed in a biological safety cabinet in the BRRAT BSL-3 laboratory with both BRRAT laboratory scientists present. The first laboratory scientist was primarily involved in performing the extraction, and the second was there to observe and learn the procedure. Both were jointly involved in filtering material, plating onto media, and reading sterility plates at 24 hours. After 24 hours of incubation, they observed no growth on any of the 16 sterility plates that had been prepared after 10 minutes of formic acid treatment. The first laboratory scientist planned to autoclave the plates, then discard them; however, the individual had difficulty opening the autoclave door. As a result, the plates were returned to the incubator and left for 7 additional days.

The first laboratory scientist moved the extracts from the BRRAT laboratory BSL-3 lab to an adjoining BSL-2 laboratory that is also part of the BRRAT laboratory. At this point, the protein extracts had been held in the formic acid/acetonitrile solution for 24 hours. The first laboratory scientist then continued with the process of preparing the material for analysis by MALDI-TOF, and then moved preparations or aliquots of the protein extracts made from the BRRAT's BSL-2 laboratory to the BSPB and BCFB laboratories on three separate days: June 6, June 11, and/or June 12, 2014.

On June 13, 2014, the second BRRAT laboratory scientist removed the sterility testing plates after 8 days in the BSL-3 incubator for autoclaving and disposal and discovered growth on the sterility plate that had been plated with unfiltered *B. anthracis*. The growth was confirmed as *B. anthracis* by real-time polymerase chain reaction using the LRN *B. anthracis* identification assays. It is not known at what point after the initial 24 hour incubation period that growth occurred. If the plates had been autoclaved after 24 hours, as planned, the event would not have been discovered.

The incident was immediately reported to the CDC Select Agent Program Responsible Official within CDC's Environment, Safety and Health Compliance Office (ESHCO) and DSAT.

CDC personnel decontaminated the affected rooms using the liquid decontamination methods described above (see Background). Laboratory floors, benchtops, equipment, and other affected areas (e.g., room door handles) were decontaminated as part of this process. Two potentially affected refrigerators were moved to a secure BSL-3 facility and decontaminated using vapor phase hydrogen peroxide. Rooms will remain closed until the procedures have been validated as EPA compliant by an external safety expert.

After the incident was discovered, two laboratory studies were undertaken to determine if the formic acid and acetonitrile treatment was effective at inactivating laboratory specimens of *B. anthracis*: one at CDC and one at an independent LRN laboratory at the Michigan Department of Community Health (MDCH). The CDC study evaluated the effect of treatment exposure times of 10 minutes in formic acid and after 6 hours and 24 hours in formic acid/acetonitrile on *B. anthracis* vegetative cells. In addition, the CDC study evaluated treatment exposure times of 10 minutes in formic acid and 24 hours in formic acid/acetonitrile using high-concentrations of *B. anthracis* spores. Cultures from treated cells and spores were monitored daily for viability for up to 8 days post-treatment. The MDCH study independently evaluated the efficacy of the formic acid/acetonitrile treatment on *B. anthracis* vegetative cells. This study used samples that were taken at three different time points: immediately on addition of the formic acid and subsequently at 1 hour and 24 hours post-treatment. The MDCH cultures were monitored for up to 8 days for viability.

Findings from both the CDC internal study and the MDCH indicate that the formic acid and formic acid/acetonitrile treatment were effective at inactivating vegetative cells of *B. anthracis*. No viable material was recovered from formic acid and formic acid/acetonitrile treated cells. These findings were consistent for the 8-day study duration. The formic acid and formic acid/acetonitrile treatments were effective at inactivating a high percentage, but not all, *B. anthracis* spores. From a starting suspension of 50,000 *B. anthracis* spores (500,000 per milliliter), which had been treated for 24 hours with the extraction process, there were a total of four colony forming units of growth in the 8-day study period.

Based on review of all aspects of the incident, it appears that while exposure of staff to viable *B. anthracis* was not impossible, it is extremely unlikely that this occurred. All or the great majority of *B. anthracis* cells and spores in the sample would have been inactivated by the 24-hour treatment (versus the 10 minute sample which grew anthrax at some point between day 2 and day 8 of incubation).

Findings

Incident-related Findings

The overriding factor contributing to this incident was the lack of an approved, written study plan reviewed by CDC senior staff, such as laboratory, branch, or division scientific leadership, to ensure that the research design was appropriate and met all laboratory safety requirements. The first BRRAT laboratory scientist was trained to work in the BSL-3 environment, including training in pathogen-specific procedures for the work normally performed. However, the individual had not performed this specific procedure with pathogenic select agents (the procedure was new to the laboratory) and should not have been instructed to proceed without submitting a complete protocol for review and approval. Further, a written protocol to certify the sterility of material to be transferred to BSL-2 laboratories was not in place, and the BSL-2 laboratories did not have an SOP that required receipt of written certification of non-viability for transfers prior to acceptance of microbiologic material. There was also inadequate supervisory oversight of a relatively new laboratory scientist performing a new experiment with virulent strains.

The first laboratory scientist also assumed that the protocol was appropriate for *B. anthracis*. It appears that there was incomplete communication between the two BRRAT laboratory scientists and the BSPB laboratory scientist about what was planned by the BRRAT laboratory and what had previously been done by the BSPB laboratory. The procedure used by the BSPB laboratory for *Brucella* species did not include a filtration step because the BSPB laboratory determined it was not necessary for extracts of *Brucella* based on the sterility testing they had done on extract material of three species of *Brucella*. Since *B. anthracis* forms spores that are more resistant to inactivation by chemicals than vegetative cells, the BRRAT laboratory scientist's assumption that the same treatment would apply to *B. anthracis* was incorrect.

The BRRAT laboratory scientist did not plan to filter extracts because it was not part of the BSPB laboratory protocol. The BRRAT laboratory scientist was aware that all DNA preparations of *B. anthracis* were filtered before leaving the BSL-3 laboratory, but assumed that it was not necessary for MALDI-TOF preparations because a filtration step was not included in the protocol. The BRRAT laboratory scientist had no previous experience transferring select agent-derived materials, other than transferring DNA preparations, from BSL-3 to BSL-2 laboratories. The BRRAT laboratory's SOP for assuring sterility was specific for DNA preparations, and SOPs for other materials do not appear to have been in place. The SOP for DNA preparations (with which the first BRRAT laboratory scientist was familiar) indicated that sterility check plates for *B. anthracis* should be held for 24-48 hours.

It is not clear that waiting 48 hours rather than 24 hours to transfer the extracts would have prevented this incident. The bacterial cells or spores were damaged by the extraction procedure, and the direct plating of the extract carried over chemicals which could have inhibited growth. Acceptable practice would have been to utilize validated methods to confirm sterility.

The following actions contributed to the incident:

1. **Use of unapproved sterilization techniques:** Staff in the BRRAT laboratory used sample preparation techniques for protein extraction from the manufacturer of the MALDI-TOF equipment, modified by the BSPB laboratory for non-spore forming bacteria (*Brucella* species) to sterilize *B. anthracis*, a

spore-forming bacterium. A laboratory scientist modified the methods from the BSPB laboratory to include comparing filtration versus non-filtration in preparing 16 plates (half filtered and half not filtered). This modification was done to assess any effects on the MALDI-TOF results, not to assure sterility. The incubation period was also shortened from 48 hours to 24 hours.

2. **Transfer of material not confirmed to be inactive:** After 24 hours without observing growth on the sterility plates, the BRRAT laboratory scientist moved the extracts from the BRRAT laboratory BSL-3 laboratory to an adjoining BSL-2 laboratory, and then continued with the process of preparing the material for analysis by MALDI-TOF. The BRRAT laboratory scientist then moved the extracted materials from the BRRAT laboratory's BSL-2 laboratory to the BCFB and BSPB laboratories on three separate days: June 6, June 11, and/or June 12, 2014. There is a lack of written procedures which had been validated to reliably ensure that organisms were no longer viable prior to removing microbiological material from BSL-3 containment
3. **Use of pathogenic *B. anthracis* when non-pathogenic strains would have been appropriate for this experiment:** The BRRAT laboratory supervisor instructed the laboratory scientist to use virulent strains because of the possibility that avirulent strains might not yield the same MALDI-TOF profile. However, the instrument manufacturer states that the system identifies bacteria to only the species level and would not distinguish strains of the same species. The use of avirulent strains to develop protocols would have been appropriate, particularly when conducting a pilot study.
4. **Inadequate knowledge of the peer-reviewed literature by the BRRAT laboratory supervisor and scientist who performed the extraction:** A review of the literature would have found that filtration has been recommended for inactivation of *B. anthracis*. There are at least two peer-reviewed publications on preparation methods for MALDI-TOF work with pathogenic bacteria, including *B. anthracis* (Drevinek et al. Letters in Applied Microbiology 2012;55:40-46; and Lasch, et al. Analytical Chemistry 2008;80:2026-2034). While the chemicals used to process the samples differ in the two publications, both required filtration of *B. anthracis* material with a 0.1 micron filter to remove spores. Drevinek et al. (2012) concluded that the formic acid method (as used by the BRRAT laboratory) did not sterilize *B. anthracis*; they also used centrifugal filtration to remove viable particles (including spores) from *B. anthracis* preparations.
5. **Lack of a standard operating procedure or process to document inactivation in writing in the BRRAT laboratory:** With correct SOPs in place that are adhered to by staff, microbiological material would have been successfully inactivated prior to transfer to a lower containment laboratory (either intra- or inter-facility) and a record of non-viability would have been provided to the receiving laboratory; also, a written record of non-viability would have been provided prior to receipt and utilization of the microbiological materials in the BSL-2 laboratories.

Response-related Findings

On June 13, 2014, two CDC staff members went to the emergency department at Emory University where they were assessed; neither presented with symptoms related to anthrax. Staff were assessed based on their risk of potential exposure that could lead to inhalational anthrax. The number of potentially exposed staff evolved as understanding of the laboratory events unfolded. Additional potentially exposed individuals were identified through supervisor discussions with individuals believed to have handled or been in proximity to the *B. anthracis* material. The process of identification was slowed by multiple factors, including the evolving nature of understanding of the event. Technology

resources such as card key readers and security video were utilized to expand the pool of potential exposures, but this was not an immediate step in the response. Even with the use of available data, several factors made the identification process difficult, including the practice of authorized staff piggy backing (obtaining entrance to a secured area by following a colleague rather than by having all individuals swipe their own card key as should be done) and incomplete or inaccurate information collected from laboratory scientists reporting their path of travel with the material between labs. Protocols were not in place for the rapid identification of potentially exposed staff, possibly delaying the use of available data sources including card key readers, visitor logs, and security video logs.

Immediate and comprehensive actions were taken to identify the potentially affected laboratory rooms as well as the individuals that were or may have been in, or traveled through, these areas during the time period of possible exposure. After ascertaining the precise events that took place in the laboratories and characterizing people's possible exposure was difficult and evolving, there were serious reservations on the part of some staff members of the affected laboratories and others about broad communication until sufficient information was gathered and verified. In retrospect, it is clear that broad communications should have occurred earlier in the process, even if more complete information was not yet available. CDC scientists who worked near the impacted laboratories commented that they first learned of the event by witnessing CDC closing and/or decontaminating laboratories rather than through direct communication regarding the ongoing event. In addition, there were inconsistencies in the decontamination practices used after the incident, which made it difficult to ensure proper methods were used. Individuals also reported the CDC clinic was overwhelmed at times during the response.

The nature of this incident required involvement of many parties from across CDC. While the roles of the responders were generally clear and appropriate actions were taken, there was no clear overall lead for the incident in the first week. This resulted in uncertainty regarding who was responsible for making decisions and taking action.

As of July 10, 2014, no staff members are believed to have become ill with anthrax.

Actions Already Underway and Plans for the Future

A moratorium was initiated July 11, 2014, on any biological material leaving any CDC BSL-3 or BSL-4 laboratory in order to allow sufficient time to put adequate improvement measures in place. In addition, CDC has already begun steps to protect staff and prevent similar incidents in the future. Key actions are planned to address the root causes of this incident. The recommendations focus on specific actions that provide redundant safeguards across the agency.

These actions and recommendations relate to

- The BRRAT laboratory
- Inactivation and transfer procedures of virulent pathogens throughout CDC laboratories
- Broader improvements in biosafety in laboratories throughout CDC
- CDC response to internal incidents
- Broader implications for the use of select agents, including for CDC's regulatory functions through CDC's Division of Select Agents and Toxins.

The BRRAT Laboratory

1. The laboratory has been closed since June 16, 2014, and will remain closed as it relates to work with any select agent. This action was reinforced by USDA's Animal and Plant Health Inspection Services (APHIS). Laboratory scientists do not have access to select agents, which have been placed in storage-only mode. The unit will remain closed with respect to select agents until the following is completed:
 - a. An assessment and appropriate follow-up actions for all BRRAT laboratory staff to determine level of skills, training, supervision, knowledge, and expertise at all levels of the organization
 - b. The establishment of clear, proven procedures that have been communicated to all staff for inactivation and non-viability testing of all types of materials that may be produced by the laboratories (i.e., not limited to nucleic acid preparations from one specific laboratory) and documentation of these processes
 - c. Resolution of all findings included in this report and in the APHIS investigation report
2. Appropriate personnel action will be taken with respect to individuals who contributed to or were in a position to prevent this incident.

Inactivation and Transfer Procedures of Virulent Pathogens throughout CDC Laboratories

3. All inactivation procedures for laboratories working with select agents and other dangerous pathogens are being carefully reviewed and will be updated as needed. This includes, but is not limited to, any inactivation performed in conjunction with MALDI-TOF testing. CDC will notify the MALDI-TOF manufacturer and the Food and Drug Administration (FDA) of this event and encourage the development of informational materials that are clearer regarding appropriate inactivation procedures for all types of pathogens. All CDC laboratories that handle select agents and other dangerous pathogens will be confirmed to have written, validated, and verified procedures to assure materials are non-viable before being removed from containment and to assure the provision of written documentation of non-viability, including the method used, for intra- and inter-facility transfers. These procedures will include requirements that all transferring laboratories confirm non-

viability by proven, effective methods before material leaves the containment laboratory and provide documentation to accompany the transfer and that the receiving laboratory confirm the materials are not viable. When new procedures, techniques, or manufacturer methods are being considered, they must first be reviewed and evaluated through a formal process to assess their risk and incorporate them into standard CDC policies, procedures, and practices prior to implementation.

Laboratories across CDC

4. CDC will establish a lead laboratory science position to be the CDC-wide single point of accountability for laboratory safety. The creation of a single point of accountability does not reduce the responsibility of people at every level of the organization, including center, division, and branch directors, chiefs, supervisors, and all laboratory scientists to strengthen the culture of safety. This position will:
 - a. Establish and enforce agency-wide policies that require formal review and approval of new select agent research or program protocols and provide oversight for ongoing research and program projects (e.g., yearly reviews).
 - b. Create effective and redundant systems and controls for protocols and procedures including, but not limited to, inactivation and access to laboratories (e.g., “piggybacking” and visitor access).
 - c. Ensure adherence to laboratory quality and safety protocols (e.g., quality assurance that biological material is non-viable before it is shipped from CDC select agent laboratories). These protocols will be transferred to new staff whenever there is a turnover in select agent laboratories, especially when there is a new principal investigator.
 - d. Review and monitor the implementation of training policies and procedures for new and existing staff.

5. Use an approach that identifies the points in any project where potential mistakes would have the most serious consequences that provides specific actions to avoid these mistakes. Examples of these critical points and associated preventive actions include requiring protocols to be reviewed by supervisors before they are implemented, having standard and clear procedures to inactivate infectious agents and specify how they will be transferred to other labs, having formal incident response plans in place, controlling laboratory access, and instituting regular review of laboratory processes to ensure proper safety, quality management, and compliances with Select Agent Regulations.
 - a. Identify ways to decrease the risk of an event such as this happening again, which may include fewer laboratories working with select agents and/or a decrease in the number of pathogenic strains being studied and/or a decrease in the number of staff members working with these agents.
 - b. Promote the use of non-pathogenic organisms in research and training activities, whenever possible.
 - c. Accelerate the ongoing implementation of laboratory quality management systems (QMS) throughout CDC laboratories. Over the past 5 years, CDC has begun implementing a QMS for infectious disease laboratories which includes document controls such as protocol archives and approval records as an integral part. Initial adoption of QMS has focused on the laboratories with clinical diagnostic responsibilities and has greatly enhanced their safety and efficiency. Expansion into nonclinical

laboratories has been ongoing and will now be accelerated as a high priority, with QMS becoming an integral part of CDC laboratory management practice.

6. CDC will establish an external advisory committee to provide ongoing advice and direction for laboratory quality and safety. It is likely this advisory committee will be established under the Federal Advisory Committee Act (FACA).

Response Efforts

7. CDC will initiate an incident command structure early in any response to an incident at CDC when an event is suspected that the incident is significant or not well understood. CDC may also leverage the assets of CDC's Emergency Operations Center to help coordinate the event response under the incident commander. This does not necessarily mean activating the EOC for such a purpose, but use of the EOC facility, staff, tools, and other resources as well as coordination within CDC offices could be beneficial. Under this structure, CDC can ensure proactive and frequent communication with staff, media, and the public. This structure will also allow for quick access to CDC staff with unique expertise to provide surge capacity (including nurses and physicians to staff the CDC clinic), as needed

Broader Implications for the Use of Select Agents

8. Lessons based on this incident that will be considered for broader implications. CDC's DSAT program will incorporate findings and recommendations into nationwide regulatory activities to provide stronger safeguards for laboratories across the United States. For example, in its review of biosafety plans with regulated entities, DSAT will emphasize the importance of having proven inactivation protocols and utilizing testing for inactivated preparations prior to distribution.

Conclusion

Potential exposure of CDC laboratory scientists to anthrax occurred as a result of a series of failures of one laboratory (the CDC BRRAT laboratory) to ensure that *B. anthracis* specimens had been inactivated before transferring them to other laboratories at CDC. This same laboratory had inadvertently transferred viable *B. anthracis* on a previous occasion in 2006. Review of the procedures and practices that allowed this event to occur identified: failures of policy, training, scientific knowledge, supervision, and judgment on the part of this laboratory. In addition, there was a lack of adequate agency-wide policies and procedures to ensure biosafety, both for decontamination of select agents and other virulent organisms as well as for biosafety more broadly. Further, biosafety policies and procedures adopted in the past were not always adhered to in the present. Response to the incident should have been better organized from the outset.

Review of the incident suggests that it is highly unlikely, but not impossible, that staff members were exposed to viable *B. anthracis*. None of the potentially exposed workers has become ill with anthrax. Nonetheless, this was a serious and unacceptable incident which should never have happened. A moratorium is being put into effect on July 11, 2014, on any biological material leaving any CDC BSL-3 or BSL-4 laboratory in order to allow sufficient time to put adequate improvement measures in place. Five key steps are being taken immediately: suspension of activities of this individual laboratory pending full review and remediation of all procedures and practices; agency-wide verification of adequate inactivation procedures; strengthening of biosafety agency-wide with appointment of a single point of accountability and through an external group of experts to review and advise CDC; improvement of management of internal incidents with use of an incident management system; and use of lessons learned from this incident to strengthen CDC's regulatory function with regard to select agents.

Given both the critical nature of investigations to enable CDC to improve our ability to detect and respond to naturally occurring and man-made events with select agents and the paramount responsibility of ensuring the safety of CDC staff members when they do this work, CDC leadership, including the CDC Director, will track the rapid and effective implementation of these plans.

Appendix A – Summary of the Inadvertent Shipment of an Influenza Virus H5N1-containing Laboratory Specimen

On July 9, 2014, CDC's select agent office and agency leadership were notified that the a low-pathogenic avian influenza sample was inadvertently cross-contaminated with a select agent, the highly pathogenic H5N1 influenza virus, before being shipped from an influenza laboratory to the US Department of Agriculture Southeast Poultry Research Laboratories (SEPRL). The H5N1 influenza was a contaminant of a low-pathogenic avian influenza virus specimen that is not a select agent. Since the influenza laboratory was unaware of the contamination, appropriate select agent transfer procedures were not followed. Because the materials were handled during shipping as 'category B' (standard shipping procedures for infectious agents) and all laboratory work in both institutions was carried out in enhanced BSL-3 facilities, there does not appear to be any safety risk posed by this incident.

Investigation of the incident thus far found that contamination of the low-pathogenic influenza virus specimen with the highly pathogenic H5N1 influenza virus occurred during laboratory work at the CDC, leading to samples being shipped without the appropriate level of permitting, notifications, or safety precautions. All work with live virus at SEPRL was conducted in their APHIS select agent approved BSL3 facilities. The ongoing investigation also has revealed unacceptable delays in reporting of the inadvertent shipment of the select agent, which was shipped on March 13, 2014, informed to CDC by SEPRL to have been contaminated on May 23, 2014, and confirmed by CDC to have been contaminated in the following days. The H5N1-containing contaminated specimens at both SEPRL and CDC have been or will be destroyed. Confirmation of the contaminated specimens was conducted without notification of the supervisory chain of command including division, center, and CDC leadership.

In response to this incident, and in conjunction with the response to the June 2014 incident of potential exposure to anthrax, CDC has initiated the following steps:

1. Established a high-level working group, reporting to the CDC Director, to, among other duties, accelerate improvements in laboratory safety; review and approve, on a laboratory-by-laboratory basis, resumed transfer of biological materials outside of BSL-3 and BSL-4 laboratories; and serve as the transition group for the single point of accountability on laboratory safety.
2. Begun the process of establishing an external advisory group for laboratory safety.
3. Initiated an investigation to determine root causes that led to contamination of another avian influenza virus by the H5N1 virus.
4. Reported the incident through the proper channels to the select agent oversight body, APHIS.
5. Established a review group, under the direction of CDC's Associate Director for Science, to look at the systems, procedures, and personnel issues leading to this event and means of preventing similar events in the future. This review will be done in conjunction with the internal investigation and in coordination with the working group.
6. Undertaking appropriate personnel action expeditiously.

Beyond these specific steps, the CDC-wide moratorium on any biological material leaving any CDC BSL-3 or BSL-4 laboratory (with effect from July 11, 2014) applies to this laboratory.

Appendix B – Timeline of Major Events

Note: Data reported below were current as of July 10, 2014.

June 5 (Thursday):

- A laboratory scientist in the Bioterrorism Rapid Response and Advanced Technology (BRRAT) laboratory prepared extracts from a panel of select agents including *B. anthracis* (Ames strain) for analysis using mass spectroscopy while in the BRRAT laboratory biosafety level 3 (BSL-3). After performing the extractions, the BRRAT laboratory worker took samples of the extracts for sterility testing after 10 minutes and continued treatment for a total 24-hour incubation.

June 6 (Friday):

- After 24 hours all plates of the extracts for sterility testing were examined by two laboratory scientists and no growth was observed. Two of these plates had *B. anthracis* (Ames strain).
- Extracts were then moved from the BRRAT laboratory BSL-3 to the BRRAT laboratory BSL-2 for further processing and preparation of a steel MALDI-TOF plate. This processing is regarded as a potential for aerosolization of the material.
- The dried MALDI-TOF plate was placed inside a plastic MALDI-TOF plate holder with a closed lid and then placed in a zip locked bag and delivered to the Biotechnology Core Facility Branch (BCFB), a BSL-2 laboratory in another building, and then taken for mass spectroscopy analysis in the BCFB laboratory.
- A laboratory scientist in BCFB laboratory noticed small flakes of material on the MALDI-TOF plate and took it to a chemical hood in that room and used a nitrogen air stream to blow off the flakes. This is regarded as a potential for aerosolization of the material.
- The MALDI-TOF plate was stored in its plastic container, with a closed lid, on the bench in BCFB Laboratory at room temperature.

June 7 - 8 (Saturday & Sunday):

- No activity related to this incident occurred. The plate was stored in its plastic container with a closed lid, on a lab bench BCFB laboratory.

June 9 (Monday):

- No activity related to this incident occurred. Plate was stored in its plastic container with a closed lid, on a laboratory bench BCFB laboratory.

June 10 (Tuesday):

- No activity related to this incident occurred. Plate was stored in its plastic container with a closed lid, on a laboratory bench BCFB laboratory.

June 11 (Wednesday):

- A laboratory scientist from the BRRAT laboratory brought a closed zip-locked bag with eight closed tubes, each tube containing 6 microliter aliquots of the extracts, from the BRRAT laboratory BSL-2 to the BCFB laboratory where it was stored in a refrigerator at +4°C. One of the tubes included an unfiltered extract prepared from *B. anthracis* on June 5, 2014.

June 12 (Thursday):

- A laboratory scientist in BCFB laboratory removed the samples from the refrigerator in the Linear Equipment Room (LER) near BCFB laboratory, and took them to another room in BCFB laboratory to be prepared under a biological hood for testing on the MALDI-TOF mass spectrometer.
- The MALDI-TOF plate was then taken to a third BCFB laboratory room, for mass spectroscopy analysis. No flaking was observed.
- A laboratory scientist in BRRAT laboratory repeated the MALDI-TOF preparation process in BRRAT BSL-2 laboratory on an open bench using extracted materials prepared on June 5, including the unfiltered *B. anthracis* extract. Preparation of the MALDI-TOF plate included vortexing the extract material, which is a potential for aerosolization of the material. The vortexing is high-powered spinning of the liquid to prepare for further testing. The dried MALDI-TOF plate was placed inside a plastic MALDI-TOF plate holder with a closed lid and then was placed in zip locked bag and delivered to the Bacterial Special Pathogens Branch (BSPB) laboratory for mass spectroscopy analysis.

June 13 (Friday):

- At 5:00 PM, a laboratory scientist in BRRAT laboratory BSL-3 was removing sterility plates from the incubator and observed growth on one plate labeled as representing *B. anthracis* (Ames strain). The identity of the organism was confirmed using real-time polymerase chain reaction (PCR) and Laboratory Response Network (LRN) approved assays. Typically, real time PCR takes ~2hours once DNA is prepared. DNA extraction can take ~45 minutes to 1 hour.
- At 5:15 PM, per the BRRAT Laboratory Incident Response Plan, the second laboratory scientist contacted the Select Agent Responsible Official (RO), who is the agency's identified official overseeing the Centers for Disease Control and Prevention's (CDC) Select Agent Compliance Program.
- At 7:00 PM, all materials distributed to other labs had been collected by BRRAT laboratory personnel and returned to BSL-3 containment. Two laboratory scientists (one from the BRRAT laboratory and one from the BCFB laboratory) were referred to Emory University Hospital Emergency Room and placed on antibiotics. Swabs were taken of affected work areas in the BRRAT laboratory and BCFB laboratory, and the work areas were then decontaminated by lab personnel.
- At 7:28PM RO contacted the BRRAT laboratory supervisor to request a status on the written summary.
- At 8:16 PM, laboratory management sent initial report of incident to the RO to support development of the content that will be entered on the Form 3 and reported to the Division of Select Agent and Toxins (DSAT)

- At 8:41 PM, RO officially notified DSAT that a release of *B. anthracis* has occurred. RO began completion of Form 3.
- At 11:07PM, CDC senior leadership were notified of incident.
- DSAT provided the United States Department of Agriculture's (USDA) Animal Plant Health Inspection Service (APHIS) with an informal notification, by phone.
- Supervisor discussions occurred to immediately identify staff who may have had any potential exposure to *B. anthracis*.
- Affected work areas in BRRAT and BCFB laboratories were decontaminated with 10% bleach for longer than 10 minutes followed by 70% ethanol.

June 14 (Saturday):

- Data were reviewed to better understand the exposure pathway and identify staff who should be assessed and placed on post-exposure prophylaxis (PEP) with antibiotics and vaccine. Initially 10 staff were identified as possibly being exposed.
- Mass spectrometers in BCFB laboratory and BSPB laboratory were shut down and will remain shut down until CDC receives advice from the manufacturer.

June 15 (Sunday):

- Further discussion occurred regarding the exposure pathway and methods to identify staff to assess and recommend for PEP.

June 16 (Monday):

- BRRAT laboratory closed.
- Further discussion occurred on the development of a risk-assessment matrix to better determine who might have been potentially exposed.
- By late Monday, staff identified the following staff as being potentially exposed to *B. anthracis*:
 - BRRAT Laboratory: 9 staff
 - BCFB Laboratory: room 1, 2 staff; room 2, 2 staff; room 3: 8 staff
 - BSPB Laboratory: 1 staff
- Distribution of antibiotics and vaccine to potentially exposed staff began.
- BCFB laboratory, room 3, was decontaminated and closed. Rooms 1 and 2 were decontaminated and deemed operational, but remain closed.
- Environmental sampling plan following LRN protocols was determined for BCFB laboratory, room 3, and BSPB laboratory.
- Exterior of the mass spectrometer in BSPB laboratory was decontaminated.
- Subject matter experts determine that staff should be placed into two exposure categories-- staff who were potentially exposed and staff who were not potentially exposed. It was not possible to gauge the level of exposure based on criteria other than presence in a room.
- It was determined that 25 individuals were potentially exposed. These staff were identified by self-referrals or supervisors/project investigators who have projects in the affected laboratories and asked to contact the clinic.

June 17 (Tuesday):

- RO formally requests Personnel Suitability Board review of all BRRAT Laboratory Tier 1 staff.
- Card readers were reviewed to assist in identifying staff who may have been in the areas where potential exposure may have occurred.
- 35 staff now determined as potentially exposed through the use of card key logs to identify the additional staff; potentially exposed staff were contacted to schedule a clinic visit.

June 18 (Wednesday):

- Environmental sampling plan developed and swabs taken in BSPB laboratory (3 locations) and in BCFB laboratory (14 locations). Plates will be observed for growth for 8 days. Following the sampling all areas were decontaminated following EPA established protocols.
- Card key logs were used to identify the additional staff, and they were contacted to schedule a clinic visit. CDC initiated a review of visitor logs: 67 individuals determined as potentially exposed based on the additional sources.

June 19 (Thursday):

- In BRRAT laboratory BSL2, floors are sprayed with Spor-Klenz[®], but due to concerns about the material damaging the equipment, lab staff requested they be provided the solution (which is stable for 7 days) and offered to clean the benches and equipment themselves.
- Personnel Suitability Board met and began to assess staff training compliance.
- On request by the CDC Director, the Office of the Associate Director for Science began internal review of the events that took place in the BRRAT laboratory on June 5 that evolved into a possible *B. anthracis* exposure event.
- DSAT briefs APHIS on the incident based upon preliminary information available.
- Form 3 completed and submitted by the RO to DSAT.

June 20 (Friday):

- Clinic hours expanded to accommodate additional staff visits to the clinic.
- DSAT provides APHIS with the Form 3.
- CDC notified of official APHIS inspection to begin on June 23 with support from DSAT inspectors.

June 21 - 22 (Saturday & Sunday)

- Formation of systematic Response Team, with workgroups established to focus on Clinical Care, Environmental Sampling, Epidemiology, Laboratory, Policy, and Communication.
- CDC laboratory studies initiated to determine if the procedures used in the BSL-3 laboratory inactivated the *B. anthracis*.

June 23 (Monday):

- Response Team convenes using the CDC Emergency Operations Center platform for logistics support.
- APHIS inspectors submit requests for information to begin paper reviews.

June 24 (Tuesday):

- In-depth risk assessment started and follow up of CDC staff and contractors potentially exposed to *B. anthracis*.
- APHIS kickoff meeting takes place.
- Additional visitors (three) self-identified as possibly exposed. They are referred to clinic for assessment. All subsequently consulted with the clinic and provided medication.

June 25 (Wednesday):

- Visitor log review completed. No new potentially exposed individuals identified to date.
- External collaborator laboratory study initiated to determine if the procedures used in the BSL-3 laboratory inactivated the *B. anthracis*.

June 26 (Thursday):

- All environmental samples taken have been observed daily and reported each time as negative after 8 days of incubation, which concludes the testing process for these samples.

June 28 - 29 (Saturday & Sunday):

- Environmental data reviewed to help inform revision of risk assessment. Results from the CDC laboratory studies and findings to date from the external collaborator laboratory study indicate that it is unlikely that viable bacteria left the BSL-3 lab.

June 30 (Monday)

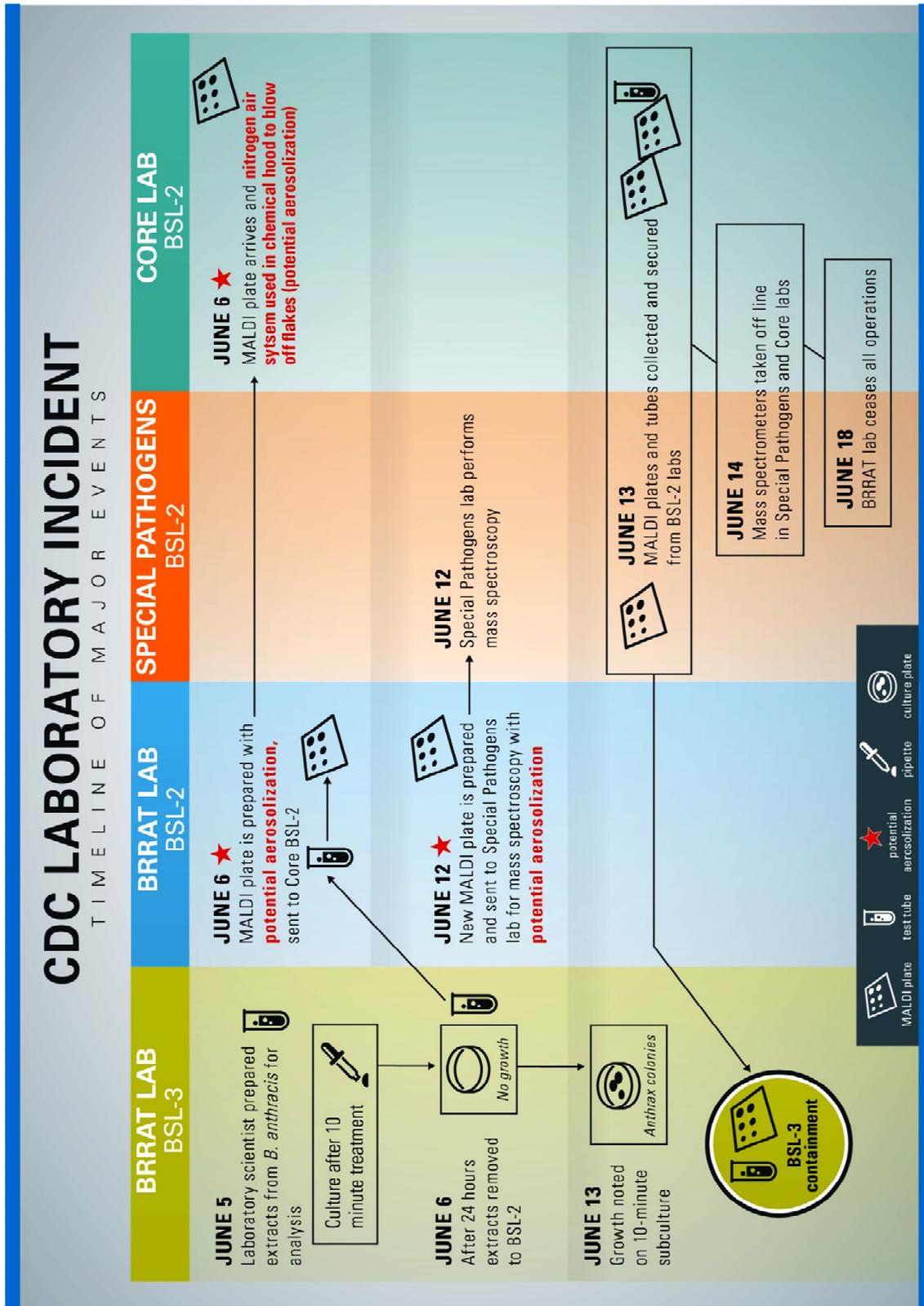
- Based on information from the laboratory studies, environmental sampling, and clinical and epidemiologic risk-assessment activities, CDC clarified potential risk groups and made new recommendations for PEP.
- To date, 29 individuals were identified as being potentially at risk because they were in affected rooms when a potential aerosolization event occurred (staff who were in a single room in the BRRAT laboratory BSL-2, on June 6 or 12; and staff who were in a single room in the BCFB laboratory, on June 6, 2014). CDC recommends that these individuals continue PEP and follow-up closely with the clinic. Any other staff who had been identified earlier as potentially exposed are determined to not be at increased risk and can discontinue or not start taking PEP. These individuals were also asked to contact the clinic for an appointment

to review their potential exposures and determine next steps. For staff on PEP determined not to have been exposed who wish still to continue PEP, the clinic will assure the availability of PEP as well as long-term health monitoring to assess adverse events.

July 7 (Monday)

- Total of 41 individuals identified as being potentially at risk. During their follow up interviews additional staff were determined to have been in the affected rooms when a potential aerosol event occurred and thus encouraged to continue PEP; these additional staff had already been recommended to start PEP as part of broader efforts to reach any potentially at risk staff.
- External laboratory obtained the same results as the CDC laboratory with regard to sterilization of vegetative cells by the method used in this incident.

Appendix C – Graphic Depiction of Major Events



Appendix D – Definitions and Terms

Animal and Plant Health Inspection Services (APHIS) – A multi-function agency within the United States Department of Agriculture (USDA) responsible for protecting and promoting U.S. agricultural health, regulating genetically engineered organisms, administering the Animal Welfare Act, and carrying out wildlife damage management activities. The Agricultural Select Agent Service (AgSAS) is part of this agency.

Biological agent – Any microorganisms (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 death, disease, or other biological malfunction in a human, an animal, a plant, or another living organism; deterioration of food, water, equipment, supplies, or material of any kind; or deleterious alteration of the environment.

Biological Select Agent and Toxin (BSAT) – Any biological agent or biological toxin that requires registration with the Federal Select Agent Program to possess, use, and transfer. In this manual, the term, “select agents and toxins,” may also be used to mean BSAT.

Biosafety Cabinet (BSC) – The primary means of containment used for working safely with infectious microorganisms that are designed to provide personnel, environmental, and product protection.

Biosafety Level (BSL) – The risk criteria used to define the four ascending levels of containment, referred to as biosafety levels 1 through 4 based on infectivity, severity of disease, transmissibility, and the nature of the work conducted.

Decontamination – The treatment of environmental surfaces (e.g., laboratory areas) to render any infectious materials sterile and nonpathogenic.

Federal Select Agent Program (FSAP) – The joint AgSAS and DSAT program responsible for administering the select agent regulations.

Inactivation – The process of treating an infectious agent to render it non-infectious and nonpathogenic.

Responsible Official (RO) – The individual designated by an entity with the authority to ensure compliance with the Select Agent Regulations at the entity.



Morbidity and Mortality Weekly Report (MMWR)

Inadvertent Laboratory Exposure to *Bacillus anthracis* --- California, 2004

Weekly

April 1, 2005 / 54(12);301-304

On June 9, 2004, the California Department of Health Services (CDHS) was notified of possible inadvertent exposure to *Bacillus anthracis* spores at Children's Hospital Oakland Research Institute (CHORI), where workers were evaluating the immune response of mice to *B. anthracis*. This report summarizes the subsequent investigation by CDHS and CDC, including assessment of exposures, administration of postexposure chemoprophylaxis, and serologic testing of potentially exposed workers. The findings underscore the importance of using appropriate biosafety practices and performing adequate sterility testing when working with material believed to contain inactivated *B. anthracis* organisms.

On May 28, 2004, CHORI staff members injected 10 mice with a suspension believed to contain nonviable vegetative cells of *B. anthracis* Ames strain. The suspension was centrifuged and drawn into syringes on an open bench in the laboratory. The mice were injected in a separate animal-handling facility at CHORI. By May 30, all of the injected animals had unexpectedly died. The carcasses were removed from the cages, placed into a plastic biohazard bag, and frozen. The bedding was discarded as standard animal waste. The cages were sanitized in an automated washer.

On June 4, an additional 40 mice were injected with the same suspension. By June 7, all but one of these mice had died. All subsequent work was performed under a biological safety cabinet (BSC), and additional personal protective equipment (PPE) was used (e.g., protective clothing and gloves). Animal cages were brought into the BSC, and the surviving animal was euthanized. The carcasses were removed, placed into double biohazard bags, and frozen. The bedding and cages were autoclaved.

On June 8, a sample of the original suspension was cultured; one mouse that died after the second experiment was necropsied and samples for cultures were obtained from its liver and peritoneal cavity. Within 24 hours, these cultures grew nonhemolytic gram-positive rods. Colony morphology was consistent with *B. anthracis*.

Suspension material and cultures were transported to a California Laboratory Response Network (LRN) reference laboratory for further identification. The California LRN confirmed that the organisms isolated were *B. anthracis* by using polymerase chain reaction and gamma phage lysis assay. At CDC, antimicrobial susceptibility testing revealed that the isolates were susceptible to penicillin, ciprofloxacin, and doxycycline. Multiple-locus variable-number tandem repeat analysis confirmed that the isolates were genotype 62, consistent with *B. anthracis* Ames strain (1).

On June 9, CDHS personnel visited the laboratory and animal-handling facility at CHORI to review the incident and laboratory procedures. No spills, puncture wounds, animal bites, or

scratches were identified; however, initial handling of the suspension included snapping lids of microtubes, ejection of pipette tips, and centrifuging. The centrifuge tubes had snap-down tops, and the rotor was covered with a gasket. The laboratory procedures might have potentially expelled small drops of suspension but were considered unlikely to have released infectious aerosols. Because staff members believed they were working with inactive organisms, they had performed these activities on an open bench, and appropriate PPE was not consistently used until after the deaths of the second group of mice.

As part of routine laboratory procedure, horizontal surfaces had been cleaned with a buffered bleach solution (1:10 dilution) at the end of each day. After laboratory workers recognized the possibility of exposure to viable *B. anthracis* spores, all laboratory surfaces and hoods were cleaned twice more with the bleach solution. The animal facility was also sanitized with bleach and a quaternary ammonium disinfectant.

Twelve persons were involved in either the laboratory or its animal-handling facilities. Three of these persons had direct contact with the bacterial suspensions, cultures, or infected animals. Although at low risk for inhalation of *B. anthracis* spores, to further reduce their risk, the three workers with direct contact were recommended for postexposure chemoprophylaxis for prevention of inhalational anthrax (i.e., either ciprofloxacin 500 mg or doxycycline 100mg, orally twice daily for 60 days) (2). The nine persons who worked in the laboratory or animal-handling facility but who did not have direct contact were offered the same chemoprophylaxis regimen. All 12 were additionally offered, but declined, anthrax vaccine under an Investigational New Drug (IND) protocol for postexposure prophylaxis (3).

Eight of the 12 potentially exposed persons opted to take chemoprophylaxis, including the three persons for whom the regimen was recommended. One person subsequently had a rash consistent with adverse reaction to ciprofloxacin; doxycycline was substituted. No other adverse effects from chemoprophylaxis were reported. None of the potentially exposed persons had symptoms consistent with anthrax.

Serum specimens collected from nine (75%) of the 12 exposed persons 3--6 weeks after exposure were negative for IgG antibodies to *B. anthracis* protective antigen (PA) by enzyme-linked immunosorbent assay (4). Three persons did not provide sera for evaluation, including one person who had direct exposure to the bacterial suspensions and cultures.

Further investigation revealed that the suspension had been prepared by a separate contract laboratory in March 2004 and contained an estimated 1.5×10^9 vegetative organisms per 1 mL of phosphate-buffered saline solution. After heating the suspension at 140°F (60°C) for 2 hours, the contractor reported that the suspension revealed no spores and had no growth after 48 hours of incubation on sheep blood agar.

A sealed, screw-top tube containing the suspension was shipped to CHORI in a double-compartment package on wet ice and arrived intact. The tube of suspension was stored in a refrigerator until used. The suspension had been prepared specifically for the research laboratory and was not distributed to other facilities. All contractor laboratory personnel had received anthrax vaccine, and the suspension was prepared under biosafety level 3 (BSL-3) conditions.

Leftover suspension from the incidents at the research laboratory were provided to CDC for quantification of viable organisms and to confirm the presence of *B. anthracis* spores. Sample dilutions were plated in duplicate on sheep blood agar. Approximately 2.0×10^6 colony-forming units (CFU) were enumerated per milliliter of suspension after 24 hours of incubation at 98.6°F (37.0°C). Comparisons of heat-shocked (149°F [65°C] for 30 minutes) and non--heat-shocked samples at CDC indicated that the suspension primarily contained *B. anthracis* spores.

Reported by: A Lucas, PhD, Children's Hospital Oakland Research Institute; M Doane, MD, J Rosenberg, MD, D Gilliss, MD, P Duffey, PhD, D Sesline, DVM, D Lindquist, MPH, R Das, MD, B Materna, PhD, D Vugia, MD, California Dept of Health Svcs. S Reagan, MPH, M Fischer, MD, N Marano, DVM, A Hoffmaster, PhD, V Semenova, PhD, S Martin, MT, C Quinn, PhD, Div Bacterial and Mycotic Diseases; J Patel, PhD, Div of Healthcare Quality Promotion, National Center for Infectious Diseases; M Kiefer, R Ehrenberg, National Institute for Occupational Safety and Health; R Weyant, PhD, Office of Health and Safety; B Ellis, PhD, T Jones, L Bane, M Hemphill, PhD, Office of Terrorism Preparedness and Emergency Response, Office of the Director, CDC.

Editorial Note:

The findings in this investigation indicate that workers in a research laboratory unknowingly received and used a suspension from a contract laboratory that likely contained viable *B. anthracis* organisms. Manipulation of the suspension at the research laboratory was determined unlikely to have expelled infectious aerosols, and exposed workers were considered at low risk for inhalation of spores. CDC continues to work with state agencies and other federal agencies to investigate processing procedures at the contractor facility to determine why the suspension contained viable *B. anthracis* organisms.

B. anthracis spores are highly resistant to the effects of heat and chemical disinfection (5). Although the heat-killing procedures used by the contractor might have been lethal to vegetative cells, the procedures were not lethal to spores. Modifying suspension preparations by increasing the temperature and duration of heat-killing procedures or using formalin will increase the probability that spores are inactivated (5,6).

Inactivated suspensions of *B. anthracis* should be cultured both at the preparing laboratory before shipment and at the research laboratory several days before use to ensure sterility. Sensitivity of sterility testing might be enhanced by increasing the inoculum size and incubation time, and by inoculating in multiple media, including both solid and broth media. Such procedures would increase the probability of detecting even a small number of viable *B. anthracis* spores. CHORI staff members did not perform sterility testing on the suspension received in March 2004.

Because inhalation of viable *B. anthracis* spores can result in fatal infection, CDC recommends that laboratory personnel who routinely perform activities with clinical materials and diagnostic quantities of infectious cultures implement BSL-2 practices (7). These practices include use of appropriate PPE (e.g., gloves, gowns, or laboratory coats) and a BSC for procedures with the potential to expel infectious aerosols (e.g., centrifuging or ejection of pipette tips). Face protection (e.g., goggles, face shield, or splatter guard) should be used against anticipated splashes or sprays when potentially infectious materials require handling outside of the BSC. In the incidents described in this report, because CHORI staff members believed they were working with nonviable organisms, they did not fully implement BSL-2 practices until after the deaths in the second group of mice.

Research laboratory workers should assume that all inactivated *B. anthracis* suspension materials are infectious until inactivation is adequately confirmed. BSL-2 procedures should be applied to all suspension manipulations performed before confirming sterility. After sterility is confirmed, laboratory personnel should continue to use BSL-2 procedures while performing activities with a high potential for expelling aerosolized spores.

The Advisory Committee on Immunization Practices recommends routine anthrax vaccination of persons who work with production quantities or concentrations of *B. anthracis* cultures or perform

other activities with a high potential for producing infectious aerosols (8). Facilities performing such work should have appropriate biosafety precautions in place to prevent exposure to *B. anthracis* spores; however, anthrax vaccination can be an additional layer of protection in the event of an unrecognized breach in practices or equipment failure. Because of the small potential for inadvertent exposure to aerosolized *B. anthracis* spores before or after sterility testing, vaccination might also be considered for researchers who routinely work with inactivated *B. anthracis* suspensions.

In addition, laboratories working with inactivated *B. anthracis* organisms should develop and implement training activities and incident-response protocols to ensure appropriate actions are taken in the event of a potential exposure. These protocols should describe mechanisms for offering counseling and postexposure chemoprophylaxis and obtaining paired sera from potentially exposed persons. Training at animal research facilities should emphasize prompt communication between animal handlers and researchers if animals are unexpectedly found dead and any special handling procedures are needed for carcasses and bedding. Finally, institutional biosafety committees should routinely review protocols and procedures to ensure that appropriate safety precautions are always in place.

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DEC 22 2008

TO: Julie Louise Gerberding, M.D., M.P.H.
Director
Centers for Disease Control and Prevention

FROM: Daniel R. Levinson *Daniel R. Levinson*
Inspector General

SUBJECT: Review of Select Agent [REDACTED] (b)(3) 42 USC 262a(h)
[REDACTED] (b)(3) 42 USC 262a(h) (A-02-07-02010)

The attached final report provides the results of our review of select agent transfers to and from the Centers for Disease Control and Prevention (CDC) [REDACTED] (b)(3) 42 USC 262a(h)
[REDACTED] (b)(3) 42 USC 262a(h)

CDC's Division of Select Agents and Toxins (DSAT) is responsible for regulating select agents and toxins (referred to as "select agents"), which are biological materials that have the potential to pose a severe threat to public health and safety. Government agencies, research organizations, and legal entities that use, possess, or transfer select agents must register with DSAT and comply with select agent regulations. (We refer collectively to these organizations as "entities.") Entities may authorize access to select agents only to individuals approved by the Secretary based on a security risk assessment by the Attorney General (referred to as "approved individuals"). Also, entities must develop and implement written security plans designed to safeguard select agents. Entities use the CDC Request To Transfer Select Agents and Toxins form (Form 2) to initiate select agent transfers, obtain DSAT approval, and document receipt of select agents.

The objective of our review was to determine whether only approved individuals accessed select agents transferred to and from [REDACTED] (b)(3) 42 USC 262

[REDACTED] (b)(3) 42 USC 262a(h)

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(b)(3)-42 USC 262a(n)

We recommend that CDC direct DSAT to:

- ensure that only approved individuals accept delivery of select agent packages by:
 - requiring entities that ship select agents via common carrier to (1) use restricted service and (2) include on the common carrier’s shipping label the names of a minimum of two approved individuals and
 - amending Form 2 to include the name of the common carrier that will provide restricted service and the name of the individual who accepted delivery of the select agent package from the common carrier;
- require all entities registered to use, possess, or transfer select agents to implement security plan procedures designed to identify and mitigate the risk that unapproved individuals might sign for and accept delivery of select agent packages from common carriers; and
- strengthen its monitoring efforts by:
 - amending its site inspection process to include a review of procedures for initial acceptance of select agent packages from common carriers and
 - implementing follow-up procedures to verify that only approved individuals signed for and accepted delivery of select agent packages from common carriers.

In its comments on our draft report, CDC concurred in principle with our recommendation to require entities that ship select agents via common carrier to (1) use restricted service and (2) include on the common carrier’s shipping label the names of a minimum of two approved

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individuals. CDC stated that it would carefully evaluate the advantages and disadvantages of implementing that recommendation. CDC fully concurred with our other recommendations.

This report contains restricted, sensitive information that may be exempt from release under the Freedom of Information Act, 5 U.S.C. § 552. The report will not be posted on the Internet. If information in the report is released pursuant to a request under the Act, the restricted, sensitive information and other information exempt from release will be redacted.

Please send us your final management decision, including any action plan, as appropriate, within 60 days. If you have any questions or comments about this report, please do not hesitate to call me, or your staff may contact Lori S. Pilcher, Assistant Inspector General for Grants, Internal Activities, and Information Technology Audits, at (202) 619-1175 or through e-mail at Lori.Pilcher@oig.hhs.gov. Please refer to report number A-02-07-02010 in all correspondence.

Attachment

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Department of Health and Human Services

**OFFICE OF
INSPECTOR GENERAL**

REVIEW OF SELECT AGENT

(b)(3) 42 USC 262a(f)

(b)(3) 42 USC 262a(h)

**URING THE
PERIOD JANUARY 1, 2006,
THROUGH MARCH 31, 2007**



Daniel R. Levinson
Inspector General

December 2008
A-02-07-02010

Office of Inspector General

<http://oig.hhs.gov>

The mission of the Office of Inspector General (OIG), as mandated by Public Law 95-452, as amended, is to protect the integrity of the Department of Health and Human Services (HHS) programs, as well as the health and welfare of beneficiaries served by those programs. This statutory mission is carried out through a nationwide network of audits, investigations, and inspections conducted by the following operating components:

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The Office of Audit Services (OAS) provides auditing services for HHS, either by conducting audits with its own audit resources or by overseeing audit work done by others. Audits examine the performance of HHS programs and/or its grantees and contractors in carrying out their respective responsibilities and are intended to provide independent assessments of HHS programs and operations. These assessments help reduce waste, abuse, and mismanagement and promote economy and efficiency throughout HHS.

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Notices

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OFFICE OF AUDIT SERVICES FINDINGS AND OPINIONS

The designation of financial or management practices as questionable, a recommendation for the disallowance of costs incurred or claimed, and any other conclusions and recommendations in this report represent the findings and opinions of OAS. Authorized officials of the HHS operating divisions will make final determination on these matters.

EXECUTIVE SUMMARY

BACKGROUND

The Public Health Security and Bioterrorism Preparedness and Response Act of 2002, Public Law 107-188, requires the Department of Health and Human Services (HHS) to regulate select agents and toxins (referred to as “select agents”), which are biological materials that have the potential to pose a severe threat to public health and safety. Within HHS, this responsibility has been assigned to the Centers for Disease Control and Prevention (CDC), Division of Select Agents and Toxins (DSAT). In collaboration with the U.S. Department of Agriculture, DSAT establishes select agent regulations and monitors and enforces compliance with the regulations.

Any government organization (Federal, State, or local), academic institution, research organization, or other legal entity that uses, possesses, or transfers select agents must register with DSAT and comply with select agent regulations. (We refer collectively to these organizations as “entities.”) Pursuant to 42 CFR § 73.10(a), entities may authorize access to select agents only to individuals approved by the HHS Secretary based on a security risk assessment by the Attorney General (referred to as “approved individuals”). Also, 42 CFR § 73.11(a) states that entities must develop and implement written security plans designed to safeguard select agents against unauthorized access, theft, loss, or release.

(b)(3) 42 USC 262a(h)

OBJECTIVE

The objective of our review was to determine whether only approved individuals accessed select agents transferred to and from § 42 USC 262.

SUMMARY OF FINDINGS

(b)(3) 42 USC 262a(n)

(b)(3) 42 USC 262a(h)

RECOMMENDATIONS

We recommend that CDC direct DSAT to:

- ensure that only approved individuals accept delivery of select agent packages by:
 - requiring entities that ship select agents via common carrier to (1) use restricted service and (2) include on the common carrier's shipping label the names of a minimum of two approved individuals and
 - amending Form 2 to include the name of the common carrier that will provide restricted service and the name of the individual who accepted delivery of the select agent package from the common carrier;
- require all entities registered to use, possess, or transfer select agents to implement security plan procedures designed to identify and mitigate the risk that unapproved individuals might sign for and accept delivery of select agent packages from common carriers; and
- strengthen its monitoring efforts by:
 - amending its site inspection process to include a review of procedures for initial acceptance of select agent packages from common carriers and
 - implementing follow-up procedures to verify that only approved individuals signed for and accepted delivery of select agent packages from common carriers.

CENTERS FOR DISEASE CONTROL AND PREVENTION COMMENTS

In its comments on our draft report, CDC concurred in principle with our recommendation to require entities that ship select agents via common carrier to (1) use restricted service and (2) include on the common carrier's shipping label the names of a minimum of two approved individuals. CDC stated that it would carefully evaluate the advantages and disadvantages of implementing that recommendation. CDC fully concurred with our other recommendations.

CDC's comments, except for technical comments, are included as Appendix B.

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INTRODUCTION

BACKGROUND

The Public Health Security and Bioterrorism Preparedness and Response Act of 2002, Public Law 107-188, requires the Department of Health and Human Services (HHS) to regulate select agents, which are biological materials that have the potential to pose a severe threat to public health and safety. Within HHS, this responsibility has been assigned to the Centers for Disease Control and Prevention (CDC), Division of Select Agents and Toxins (DSAT). In collaboration with the U.S. Department of Agriculture, DSAT establishes select agent regulations and monitors and enforces compliance with the regulations.¹

Any government agency (Federal, State, or local), academic institution, research organization, or other legal entity that uses, possesses, or transfers select agents must register with DSAT and comply with select agent regulations. (We refer collectively to these organizations as “entities.”)

Select Agent Regulations

Pursuant to 42 CFR § 73.10(a), entities may authorize access to select agents only to individuals approved by the HHS Secretary based on a security risk assessment by the Attorney General (referred to as “approved individuals”). Also, 42 CFR § 73.11(a) states that entities must develop and implement written security plans designed to safeguard select agents against unauthorized access, theft, loss, or release. Pursuant to 42 CFR § 73.9, an entity that transfers select agents must designate a Responsible Official who has the authority and responsibility to act on behalf of the entity and ensure compliance with select agent regulations.

Select Agent Transfer Process²

Registered entities may obtain select agents from a CDC laboratory, such as (b) (3) 42 USC 262a(h) or from any non-CDC entity in the United States. Select agents are transferred between entities via common carrier³ or via hand delivery by a sending entity employee to a receiving entity employee.

¹DSAT regulates select agents and toxins that could pose a severe threat to public health and safety. The U.S. Department of Agriculture, Animal and Plant Health Inspection Service (APHIS), regulates select agents and toxins that could pose a severe threat to animal or plant health. DSAT and APHIS coordinate regulatory activities for those agents that affect both humans and animals (known as overlap select agents and toxins). For purposes of this report, “select agents” refers to all agents and toxins covered under CDC regulations (42 CFR §§ 73.3 and 73.4).

²We obtained information on the select agent transfer process from 42 CFR § 73.16 and interviews with officials of (b) (3) 42 USC 262a(h)

³Common carriers, which offer transportation services at established rates, are regulated by the U.S. Department of Transportation (DOT) and are not subject to 42 CFR § 73. Therefore, common carrier employees are not required to be approved individuals.

OBJECTIVE, SCOPE, AND METHODOLOGY

Objective

The objective of our review was to determine whether only approved individuals accessed select agents transferred to and from (b) (3) 42 USC 262

Scope

Our audit covered select agent transfers to and from (b) (3) 42 USC 262 during the period January 1, 2006, through March 31, 2007.⁶ We focused on access to select agents from the point of delivery to check-in at the laboratory at the receiving entity.

We did not perform an indepth review of DSAT's internal control structure. Rather, we reviewed pertinent DSAT controls relating to the transfer of select agents. In addition, we gained an understanding of procedures governing select agent transfers implemented by (b) (3) 42 USC 262 other entities, and common carriers involved in the transfers reviewed.

We performed our fieldwork at (b) (3) 42 USC 262a(n) from May 2007 through February 2008.

Methodology

To accomplish our objective, we:

- reviewed relevant Federal laws, regulations, and guidance;
- gained an understanding of the role of DSAT, entities, and common carriers in the select agent transfer process;
- reviewed entities' security plan procedures for the receipt of select agents;
- identified a total population of 112 select agent transfers completed during our audit period;
- obtained a list of approved individuals at the entities that received the transferred select agents;
- reviewed the common carriers' electronic tracking data to determine who signed for and accepted delivery of the 104 select agent packages delivered via common carrier;

⁶In a separate review, we are examining transfers of select agents between non-CDC entities.

- interviewed entity officials to determine who accessed the eight hand-delivered select agent packages; and
- reviewed common carriers' transportation security plans and shipping cost information.

We conducted this performance audit in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objective.

FINDINGS AND RECOMMENDATIONS

(b)(3) 42 USC 262a(f)

(b)(3) 42 USC 262a(f)

(b)(3) 42 USC 262a(f)

(b)(3) 42 USC 262a(f)

(b)(3) 42 USC 262a(h)

RECOMMENDATIONS

We recommend that CDC direct DSAT to:

- ensure that only approved individuals accept delivery of select agent packages by:
 - requiring entities that ship select agents via common carrier to (1) use restricted service and (2) include on the common carrier's shipping label the names of a minimum of two approved individuals and

¹⁰Francisella tularensis is the causative agent of rabbit fever, a highly infectious disease with severe flu-like symptoms.

- amending Form 2 to include the name of the common carrier that will provide restricted service and the name of the individual who accepted delivery of the select agent package from the common carrier;
- require all entities registered to use, possess, or transfer select agents to implement security plan procedures designed to identify and mitigate the risk that unapproved individuals might sign for and accept delivery of select agent packages from common carriers; and
- strengthen its monitoring efforts by:
 - amending its site inspection process to include a review of procedures for initial acceptance of select agent packages from common carriers and
 - implementing follow-up procedures to verify that only approved individuals signed for and accepted delivery of select agent packages from common carriers.

CENTERS FOR DISEASE CONTROL AND PREVENTION COMMENTS

In its comments on our draft report, CDC concurred in principle with our recommendation to require entities that ship select agents via common carrier to (1) use restricted service and (2) include on the common carrier's shipping label the names of a minimum of two approved individuals. CDC stated that it would carefully evaluate the advantages and disadvantages of implementing that recommendation. CDC fully concurred with our other recommendations. CDC also provided technical comments, which we addressed as appropriate.

CDC's comments, except for technical comments, are included as Appendix B.

OTHER MATTERS

(b)(3) 42 USC 262a(h)

SELECT AGENT PACKAGING REQUIREMENTS

Pursuant to CDC regulations (42 CFR § 73.16(i)), an entity that transfers a select agent to another entity must comply with all applicable packaging and shipping laws. DOT regulations (49 CFR § 173.134) classify infectious substances as Category A or B substances and provide packaging requirements for each category. Category A includes substances that are shipped in a form capable of causing death or permanent disability to humans or animals, and Category B includes all other infectious substances. DOT lists Category A infectious substances in the Federal Register ((71 Fed. Reg. 32245, 32246) (June 2, 2006)). However, this list does not include all substances classified as select agents under CDC regulations (42 CFR §§ 73.3 and 73.4), nor does it provide guidance on shipping select agents that are not listed as Category A substances. DSAT did not coordinate with DOT to ensure that entities had comprehensive guidance for packaging all select agents.

APPENDIXES

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

RECEIVED

2008 OCT -8 PM 1:00

Centers for Disease Control
and Prevention (CDC)
Atlanta GA 30333OFFICE OF THE
GENERAL

OCT 3 2008

TO: Daniel R. Levinson
Inspector General
Department of Health and Human Services (HHS)

FROM: Director
Centers for Disease Control and Prevention

SUBJECT: Office of Inspector General's Draft Report: "Review of Select Agent (b)(3) 42 USC 262a(h) (b)(3) 42 USC 262a(h) during the Period January 1, 2006 through March 31, 2007"
(A-02-07-02010)

The Centers for Disease Control and Prevention (CDC) Division of Select Agents and Toxins (DSAT) appreciates the opportunity to review and comment on the Office of Inspector General's draft report, "Review of Select Agent Transfers (b)(3) 42 USC 262a(h) during the Period January 1, 2006 through March 31, 2007." Thank you for your review of this important issue.

As stated in the draft, the objective of this review was to determine whether only approved individuals accessed select agent transfers to and from the (b)(3) 42 USC 262a(h). The draft identified four findings regarding the improperly handled transfers and also provided the following recommendations to address these findings:

Office of Inspector General (OIG) Recommendation: CDC direct DSAT to ensure that only approved individuals accept delivery of select agent packages by requiring entities that ship select agents via common carrier to (1) use restricted service and (2) include on the common carrier's shipping label the names of a minimum of two approved individuals.

DSAT Response: DSAT concurs in principle with this recommendation. In accordance with the Select Agent Regulations (42 C.F.R. Part 73, 9 C.F.R. Part 121, 7 C.F.R. Part 331), DSAT strives to ensure that shipments containing select agents and toxins are safeguarded against unauthorized access, as well as against thefts, losses, or releases. It is important to note that of the

(b)(3) 42 USC 262a(h)

Given the concerns identified by this audit and consideration of the other possible vulnerabilities that may occur during the shipment of select agents and toxins, DSAT is currently reviewing how entities ship select agents and toxins and evaluating ways to improve this process to ensure that the shipment of select agents and toxins is not only safeguarded against unauthorized access, but also

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Page 2 - Daniel R. Levinson

against theft, loss, or release.

(b)(3) 42 USC 262a(h)

(b)(3) 42 USC 262a(h)

(b)(3) 42 USC 262a(h) DSAT also wants to ensure that implementation of this recommendation will not impede research, as was mandated by the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (P.L. 107-188). DSAT will carefully evaluate the advantages and disadvantages of implementing this recommendation as currently described.

OIG Recommendation: CDC direct DSAT to ensure that only approved individuals accept delivery of select agent packages by amending Form 2 to include the name of the common carrier that will provide restricted service and the name of the individual who accepted delivery of the select agent package from the common carrier.

DSAT Response: DSAT concurs with this recommendation.

(b)(3) 42 USC 262a(h)

(b)(3) 42 USC 262a(h)

OIG Recommendation: CDC direct DSAT to require all entities registered to possess, use, or transfer select agents to implement security plan procedures designed to identify and mitigate the risk that unapproved individuals might sign for and accept delivery of select agent packages from common carriers.

DSAT Response: DSAT concurs with this recommendation. Section 73.11 of the Select Agent Regulations (42 C.F.R. 73.11) requires that an entity develop and implement a written security plan that is sufficient to safeguard the select agent or toxin against unauthorized access, theft, loss, or release. The security plan must also be designed according to a site-specific risk assessment and must provide graded protection in accordance with the risk of the select agent or toxin, given its intended use. This risk assessment should include how the entity ships and receives select agents and toxins.

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Page 3 - Daniel R. Levinson

On April 18, 2007, DSAT provided to the regulated entities informational documents to assist entities in complying with the security requirements of the Select Agent Regulations. These documents should assist entities in developing or revising a written security plan and in performing a site-specific risk assessment. The documents are available on the National Select Agent Registry (NSAR) website at <http://www.selectagents.gov/complianceAssistance.htm>.

Additional guidance is currently being developed in collaboration with the Department of Transportation to provide entities with information on the regulations governing the transportation of select agents and toxins. In addition, DSAT, in coordination with APHIS, is developing two educational workshops with the theme of "Management Oversight" to inform Responsible Officials of their legal responsibilities for implementing the Select Agent Regulations. These workshops are scheduled for Fall 2008 and Summer 2009.

OIG Recommendation: CDC direct DSAT to strengthen its monitoring efforts by amending its site inspection process to include a review of procedures for initial acceptance of select agent packages from common carriers.

DSAT Response: DSAT concurs with this recommendation. Even though DSAT inspectors received training on how to perform site inspections and were provided with a "Security" checklist for ensuring that an entity meets the security requirements of the regulations, this audit

(b)(3) 42 USC 262a(h)

(b)(3) 42 USC 262a(h)

To ensure consistency among the inspectors, DSAT has revised its standard operating procedure (SOP) involving inspections to include an expectation that inspectors review shipping and receiving protocols to determine if unapproved individuals signed for and accepted delivery of select agent packages upon initial receipt from carriers. DSAT also has improved the inspection process by having inspectors review security plans in advance of the inspection to verify that the plans include such protocols. Once on-site, the inspectors verify the information through inspection of the facility and querying the staff.

Recognizing the importance of having a well-trained inspection staff, DSAT has designated a Training Officer that oversees training activities for inspectors, conducts bi-weekly inspector training sessions, and provides information exchange to inspectors through e-mails from the DSAT Deputy Director.

OIG Recommendation: CDC direct DSAT to strengthen its monitoring efforts by implementing follow-up procedures to verify that only approved individuals signed for and accepted delivery of select agent packages from common carriers.

DSAT Response: DSAT concurs with this recommendation.

(b)(3) 42 USC 262a(h)

(b)(3) 42 USC 262a(h)

(b)(3) 42 USC 262a(h)

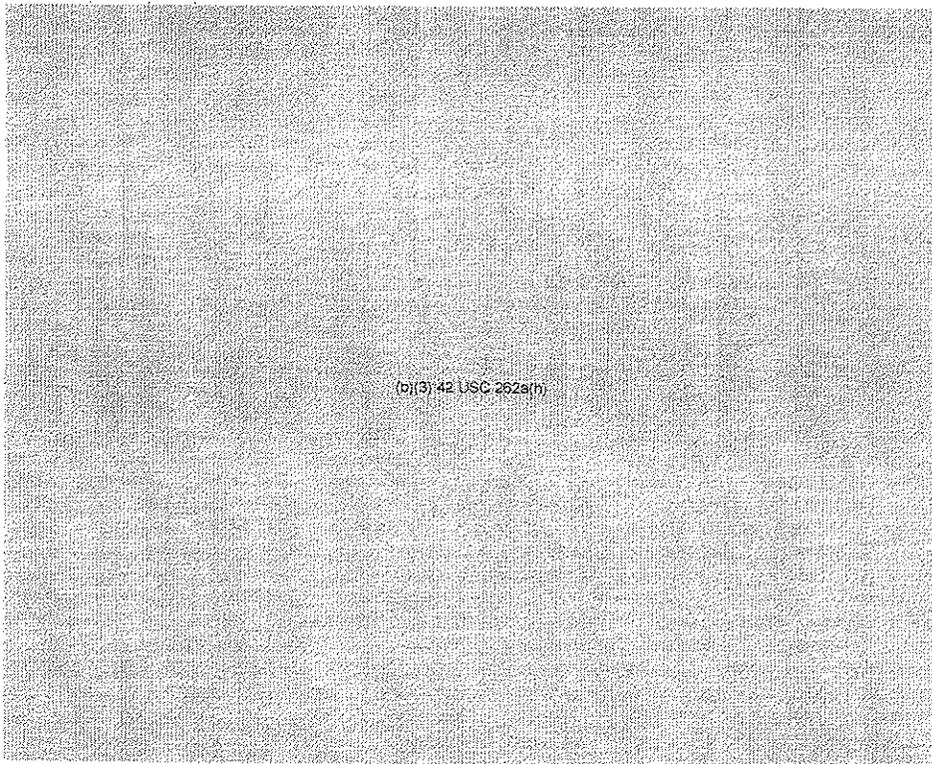
To address this recommendation, DSAT will strengthen its monitoring efforts by developing a quality control checklist that will

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Page 4 -- Daniel R. Levinson

ensure that the DSAT reviewer confirms that no unauthorized access occurred during the transfer process by checking the name of the individuals identified on the APHIS/CDC Form 2 as packaging and receiving the select agent shipment against the list of Security Risk Assessment-approved individuals at the sending and receiving entities. The changes to the APHIS/CDC Form 2 and the new follow-up procedures will make CDC and APHIS aware of any unauthorized access that may have occurred during the packaging and receipt of the select agent shipment.

OTHER MATTERS:



In addition, DSAT is working with DOT to develop guidance for the regulated community on the shipping and packaging of select agents. This guidance will include information on all applicable domestic and international shipping regulations and guidance and will be available to the regulated community via the NSAR website (www.selectagents.gov).

Technical comments on the draft report are provided in the attachment. We appreciate your consideration of the comments contained in this memo and the technical comments as you develop

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Page 5 - Daniel R. Levinson

the final report. We are happy to discuss any of these comments with you. Please direct any questions regarding these comments to Mr. Shaun Ratliff by telephone at (404) 639-2809 or by e-mail at iggao@cdc.gov.


Julie Louise Gerberding, M.D., M.P.H.

Attachment

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SEP 25 2009

TO: Thomas R. Frieden, M.D., M.P.H.
Director
Centers for Disease Control and Prevention

FROM: Joseph E. Vengrin 
Deputy Inspector General for Audit Services

SUBJECT: Review of Compliance With Select Agent Regulations by the Centers for Disease Control and Prevention, (b)(3), 42 USC 262a(h)
(b)(3), 42 USC 262a(h) (A-04-08-01060)

The attached final report provides the results of our review of compliance with select agent regulations by the Centers for Disease Control and Prevention (CDC), (b)(3), 42 USC 262a(h). This review was part of a series of reviews of Federal laboratories' compliance with select agent regulations.

Select agents are biological materials that have the potential to pose a severe threat to public health and safety. Any government agency (Federal, State, or local), academic institution, research organization, or other legal entity that possesses, uses, or transfers select agents must register with CDC and comply with Federal select agent regulations.

Our objective was to determine whether the Laboratories complied with Federal select agent regulations.

The Laboratories complied with some Federal select agent regulations. Specifically, the Laboratories had appointed a Responsible Official; restricted access to select agents to approved individuals; developed and implemented security, biosafety, and incident response plans; maintained the required inventory and access records; and complied with select agent transfer requirements. However, the Laboratories did not always ensure that individuals received select agent training before they accessed select agent areas. In addition, the Laboratories did not always comply with security plan requirements for coding electronic cards used to access select agent areas and storage freezers. These weaknesses could have compromised the Laboratories' ability to safeguard select agents from accidental or intentional loss and to ensure the safety of individuals who worked with select agents.

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We recommend that the Laboratories:

- ensure that training is provided to all individuals before granting them access to select agent areas and
- ensure that electronic access cards are coded in compliance with the Laboratories' security plan.

In its written comments on our draft report, CDC concurred with our findings. CDC provided information on actions taken to ensure that training is provided to individuals before granting them access to select agent areas and to ensure that electronic access cards are properly coded.

This report contains restricted, sensitive information that may be exempt from release under the Freedom of Information Act, 5 U.S.C. § 552. The report will not be posted on the Internet. If information in the report is released pursuant to a request under the Act, the restricted, sensitive information and other information exempt from release will be redacted.

Please send us your final management decision, including any action plan, as appropriate, within 60 days. If you have any questions or comments about this report, please do not hesitate to call me, or your staff may contact Lori S. Pilcher, Assistant Inspector General for Grants, Internal Activities, and Information Technology Audits, at (202) 619-1175 or through email at Lori.Pilcher@oig.hhs.gov. Please refer to report number A-04-08-01060 in all correspondence.

Attachment

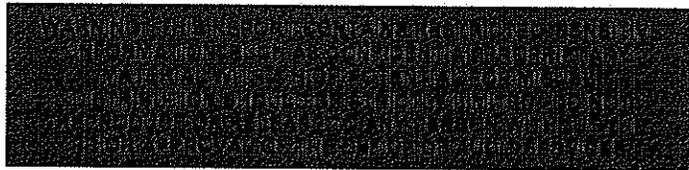
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Department of Health and Human Services

**OFFICE OF
INSPECTOR GENERAL**

**REVIEW OF COMPLIANCE WITH
SELECT AGENT REGULATIONS
BY THE CENTERS FOR DISEASE
CONTROL AND PREVENTION,**

(b)(3) 42 USC 262a(n)



Daniel R. Levinson
Inspector General

September 2009
A-04-08-01060

Office of Inspector General

<http://oig.hhs.gov>

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OFFICE OF AUDIT SERVICES FINDINGS AND OPINIONS

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EXECUTIVE SUMMARY

BACKGROUND

The Public Health Security and Bioterrorism Preparedness and Response Act of 2002, 42 U.S.C. § 262a, requires the Department of Health and Human Services (HHS) to regulate select agents, which are biological materials that have the potential to pose a severe threat to public health and safety. Within HHS, this responsibility has been assigned to the Centers for Disease Control and Prevention (CDC). In collaboration with the U.S. Department of Agriculture, CDC establishes select agent regulations and monitors and enforces compliance with the regulations.

Any government agency (Federal, State, or local), academic institution, research organization, or other legal entity that possesses, uses, or transfers select agents must register with CDC and comply with Federal select agent regulations. (We refer collectively to these organizations as “entities.”) Entities must, among other things, appoint a Responsible Official to ensure compliance with the regulations; restrict access to select agents to individuals approved by the HHS Secretary based on a security risk assessment by the Attorney General (referred to as “approved individuals”); develop and implement security, biosafety, and incident response plans; provide training on biosafety and security; maintain detailed select agent inventory and access records; and comply with select agent transfer requirements.

Following the 2001 terrorist attacks and anthrax release, we conducted a series of reviews of compliance with Federal select agent regulations by State, local, nonprofit, and university laboratories. In April 2008, we began a series of similar reviews at six Federal entities. This review, one in the series, addresses compliance by CDC

(b)(3) 42 USC 262a(h)

(b)(3) 42 USC 262a(h)

OBJECTIVE

Our objective was to determine whether the Laboratories complied with Federal select agent regulations.

SUMMARY OF FINDINGS

The Laboratories complied with some Federal select agent regulations. Specifically, the Laboratories had appointed a Responsible Official; restricted access to select agents to approved individuals; developed and implemented security, biosafety, and incident response plans; maintained the required inventory and access records; and complied with select agent transfer requirements. However, the Laboratories did not always ensure that individuals received select agent training before they accessed select agent areas. In addition, the Laboratories did not always comply with security plan requirements for coding electronic cards used to access select agent areas and storage freezers. These weaknesses could have compromised the Laboratories’ ability to safeguard select agents from accidental or intentional loss and to ensure the safety of individuals who worked with select agents.

RECOMMENDATIONS

We recommend that the Laboratories:

- ensure that training is provided to all individuals before granting them access to select agent areas and
- ensure that electronic access cards are coded in compliance with the Laboratories' security plan.

CENTERS FOR DISEASE CONTROL AND PREVENTION COMMENTS

In its written comments on our draft report, CDC concurred with our findings. CDC provided information on actions taken to ensure that training is provided to individuals before granting them access to select agent areas and to ensure that electronic access cards are properly coded. CDC also provided technical comments, which we addressed as appropriate. CDC's comments, excluding technical comments, are included as Appendix B.

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INTRODUCTION

BACKGROUND

The Public Health Security and Bioterrorism Preparedness and Response Act of 2002, 42 U.S.C. § 262a, requires the Department of Health and Human Services (HHS) to regulate select agents, which are biological materials that have the potential to pose a severe threat to public health and safety.¹ Within HHS, this responsibility has been assigned to the Centers for Disease Control and Prevention (CDC). In collaboration with the U.S. Department of Agriculture (USDA), CDC establishes select agent regulations and monitors and enforces compliance with the regulations.²

Any government agency (Federal, State, or local), academic institution, research organization, or other legal entity that possesses, uses, or transfers select agents must register with CDC and comply with Federal select agent regulations. (We refer collectively to these organizations as “entities.”)

Federal Select Agent Regulations

Federal select agent regulations (42 CFR part 73) require that entities, among other things, appoint a Responsible Official to ensure compliance with the regulations; restrict access to select agents to individuals approved by the HHS Secretary based on a security risk assessment by the Attorney General (referred to as “approved individuals”); develop and implement security, biosafety, and incident response plans; provide training on biosafety and security; maintain detailed select agent inventory and access records; and comply with select agent transfer requirements. Appendix A contains the specific Federal regulations relevant to this review.

Office of Inspector General Reviews

Following the 2001 terrorist attacks and anthrax release, we conducted a series of reviews of compliance with Federal select agent regulations by State, local, nonprofit, and university laboratories. In April 2008, we began a series of similar reviews at six Federal entities. This review is one in the series.

(b) (3); 42 USC 262a(n)

¹For purposes of this report, “select agents” refers to all agents and toxins listed in 42 CFR §§ 73.3 and 73.4.

²CDC regulates select agents that could pose a severe threat to public health and safety. USDA regulates select agents and toxins that could pose a severe threat to animal or plant health. CDC and USDA coordinate regulatory activities for those agents that affect both humans and animals (known as overlap select agents and toxins).

OBJECTIVE, SCOPE, AND METHODOLOGY

Objective

Our objective was to determine whether the Laboratories complied with Federal select agent regulations.

Scope

Our review covered the period April 18, 2005, the effective date of HHS's final rule for implementing select agent regulations,⁴ through September 30, 2008. We limited our review to 17 of the Laboratories' 72 facilities. We did not perform an indepth review of the Laboratories' internal control structure. Rather, we limited our review to controls related to the Laboratories' compliance with select agent regulations.

We performed our fieldwork [REDACTED] (b)(3) 42 USC 262a(h) from October 2008 through January 2009.

Methodology

To accomplish our objective, we:

- reviewed applicable Federal laws, regulations, and guidance;
- reviewed CDC records related to the Laboratories' registration;
- reviewed the Laboratories' select agent security plan, biosafety plan, and incident response plan;
- held discussions with officials of the Laboratories to gain an understanding of the Laboratories' policies and procedures for implementing select agent regulations;
- reviewed the Laboratories' security, biosafety, and incident response procedures;

⁴70 Fed. Reg. 13294–13325 (Mar. 18, 2005).

- reviewed the Laboratories' records related to biosafety and security training;
- reviewed the Laboratories' select agent inventory and access records; and
- reviewed the Laboratories' procedures for transferring select agents.

We conducted this performance audit in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objective.

FINDINGS AND RECOMMENDATIONS

The Laboratories complied with some Federal select agent regulations. Specifically, the Laboratories had appointed a Responsible Official; restricted access to select agents to approved individuals; developed and implemented security, biosafety, and incident response plans; maintained the required inventory and access records; and complied with select agent transfer requirements. However, the Laboratories did not always ensure that individuals received select agent training before they accessed select agent areas. In addition, the Laboratories did not always comply with security plan requirements for coding electronic cards used to access select agent areas and storage freezers. These weaknesses could have compromised the Laboratories' ability to safeguard select agents from accidental or intentional loss and to ensure the safety of individuals who worked with select agents.

SELECT AGENT TRAINING

Regulations (42 CFR § 73.15(a)) require entities to provide biosafety and security training to individuals before they access select agent areas.

The Laboratories did not provide biosafety and security training to 88 of the 168 approved individuals before granting the individuals access to select agent areas. Although the individuals subsequently received training, it was sometimes delayed by as long as 1 year. According to the Responsible Official, the delays in providing training resulted from difficulties encountered in coordinating training with human resources personnel and the principal investigators requesting the training.

SECURITY PLAN

Regulations (42 CFR § 73.11(c)) require entities to develop and implement a written security plan to safeguard select agents against unauthorized access.

The Laboratories' security plan required its Security Office to enter authorization codes on the electronic cards that approved individuals used to access select agent areas and the freezers where select agents were stored. According to the security plan, authorization was to be

restricted to the specific select agent areas and storage freezers to which each individual had been granted access. For example, security guards were granted access to select agent areas but not to the storage freezers. However, at one of the Laboratories' facilities, the authorization code that the Security Office entered on the electronic cards allowed all approved individuals to access all select agent areas and freezers, regardless of whether the individuals were approved for such access.

RECOMMENDATIONS

We recommend that the Laboratories:

- ensure that training is provided to all individuals before granting them access to select agent areas and
- ensure that electronic access cards are coded in compliance with the Laboratories' security plan.

CENTERS FOR DISEASE CONTROL AND PREVENTION COMMENTS

In its written comments on our draft report, CDC concurred with our findings. CDC provided information on actions taken to ensure that training is provided to individuals before granting them access to select agent areas and to ensure that electronic access cards are properly coded. CDC also provided technical comments, which we addressed as appropriate. CDC's comments, excluding technical comments, are included as Appendix B.

APPENDIXES

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FEDERAL SELECT AGENT REGULATIONS

- Regulations (42 CFR §§ 73.3 and 73.4) list select agents and toxins, which are biological materials that have the potential to pose a severe threat to public health and safety (referred to as “select agents” for purposes of the report and this Appendix).
- Regulations (42 CFR § 73.7(a)) require that an individual or entity not possess, use, or transfer select agents without a certificate of registration issued by the Secretary of the U.S. Department of Health and Human Services (HHS).
- Regulations (42 CFR § 73.7(b)) require each entity to designate an individual to be its Responsible Official.
- Regulations (42 CFR § 73.7(h)) require an entity to amend its registration to reflect changes in circumstances (personnel changes, changes in the activities involving any select agent, or the addition or removal of select agents).
- Regulations (42 CFR § 73.9(a)) require that the Responsible Official have the authority and responsibility to act on behalf of the entity and ensure the entity’s compliance with requirements of the select agent regulations.
- Regulations (42 CFR § 73.10(a)) require an entity to authorize access to select agents only to individuals approved by the HHS Secretary following a security risk assessment by the Attorney General (referred to as “approved individuals”).
- Regulations (42 CFR § 73.10(j)) require the Responsible Official to immediately notify the Centers for Disease Control and Prevention (CDC) (or the U.S. Department of Agriculture) when an individual’s access to select agents is terminated and the reasons for the termination.
- Regulations (42 CFR § 73.11(a)) require entities to develop and implement a written security plan. The security plan must be sufficient to safeguard select agents against unauthorized access, theft, loss, or release.
- Regulations (42 CFR § 73.11(b)) require that the entity’s security plan be designed according to a site-specific risk assessment and provide protection in accordance with the risk of the select agent, given its intended use.
- Regulations (42 CFR § 73.11(c)) require the entity’s security plan to contain procedures for physical security, inventory control, and information systems control, as well as provisions for controlling access to select agents. In addition, each entity’s plan must contain provisions for routine cleaning, maintenance, and repairs and procedures for removing unauthorized or suspicious persons. Each plan must describe procedures for addressing the loss or compromise of keys, passwords, or combinations and protocols for changing access numbers or locks following staff changes. Plans also must contain procedures for reporting unauthorized or suspicious persons or activities; the loss, theft, or release of select agents; or

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the alteration of inventory records, as well as procedures for ensuring that all approved individuals understand and comply with security procedures.

- Regulations (42 CFR § 73.11(d)) require entities to allow access to select agents only to approved individuals. However, unapproved individuals who conduct routine cleaning, maintenance, repairs, or other activities not related to select agents may access select agent areas only when continuously escorted by an approved individual. In addition, freezers, refrigerators, cabinets, and other containers where select agents are stored are required to be secured against unauthorized access. The security plan also must contain procedures for intraentity transfers of select agents, the avoidance of sharing individuals' unique means of access to select agents, and the separation of select agent areas from public areas.
- Regulations (42 CFR § 73.11(f)) require entities to review annually and revise, as necessary, their security plan. Further, entities must conduct drills or exercises at least annually to test and evaluate the effectiveness of their plan. The plan must be reviewed and revised, as necessary, after any drill or exercise and after any incident.
- Regulations (42 CFR § 73.12(a)) require entities to develop and implement a written biosafety plan that is commensurate with the risk of the agent, given its intended use. The biosafety plan must contain sufficient information and documentation to describe the biosafety and containment procedures.
- Regulations (42 CFR § 73.12(d)) require entities to review annually and revise, as necessary, their biosafety plan. Further, entities must conduct drills or exercises at least annually to test and evaluate the effectiveness of their plan. The plan must be reviewed and revised, as necessary, after any drill or exercise and after any incident.
- Regulations (42 CFR § 73.14(a)) require entities to develop and implement a written incident response plan. The incident response plan must be coordinated with any entitywide plans, kept in the workplace, and available to employees for review.
- Regulations (42 CFR § 73.14(c)) require each entity's incident response plan to contain information related to names and contact information for responsible entity and building officials, personnel roles and lines of authority and communication, planning and coordination with local emergency responders, procedures for employees performing rescue or medical duties, a list of personal protective and emergency equipment, site security and control, procedures for emergency evacuation, and decontamination procedures.
- Regulations (42 CFR § 73.14(d)) require entities to review and revise, as necessary, their incident response plans. Further, entities must conduct drills or exercises at least annually to test and evaluate the effectiveness of their plan. The plan must be reviewed and revised, as necessary, after any drill or exercise and after any incident.
- Regulations (42 CFR § 73.15(a)) require entities to provide information and training on biosafety and security to individuals before they access select agent areas.

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- Regulations (42 CFR § 73.15(b)) require entities to provide annual refresher training for approved individuals.
- Regulations (42 CFR § 73.15(c)) require entities to maintain a record of training provided to each individual. The record must include the name of the individual, the date of the training, a description of the training, and the means used to verify that the employee understood the training.
- Regulations (42 CFR § 73.16) require entities to transfer a select agent only to an entity registered to possess that particular select agent. Each transfer must be authorized by CDC (or the U.S. Department of Agriculture) before the transfer. In addition, the sender must comply with all laws concerning packaging and shipping.
- Regulations (42 CFR §§ 73.17(a)(1) and 73.17(a)(2)) require entities to maintain complete records relating to select agent inventories.
- Regulations (42 CFR § 73.17(a)(3)) require entities to maintain a current list of all approved individuals.
- Regulations (42 CFR § 73.17(a)(4)) require entities to maintain complete records related to all entries into areas containing select agents, including the name of the individual, name of the escort (if applicable), and date and time of entry.
- Regulations (42 CFR § 73.17(b)) require entities to implement a system to ensure that all records and databases created under 42 CFR part 73 are accurate, that access to them is controlled, and that their authenticity may be verified

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control
and Prevention (CDC)
Atlanta GA 30333

AUG 31 2009

TO: Joseph E. Vengrin
Deputy Inspector General for Audit Services

FROM: Thomas R. Frieden, M.D., M.P.H.
Director
Centers for Disease Control and Prevention

SUBJECT: Office of the Inspector General's Draft Report: Compliance with Select Agent Regulation – (b)(3) 42 USC 262a(h) 42 USC 26(A-04-08-01060)

The Centers for Disease Control and Prevention (CDC), (b)(3) 42 USC 262a(h) (b)(3) 42 USC 262a(h) appreciates the opportunity to review and comment on the Office of the Inspector General's (OIG) draft report entitled, "Compliance with Select Agent Regulation – (b)(3) 42 USC 262a(h) (b)(3) 42 USC 262a(h) Thank you for your review of the (b)(3) 42 USC 262a(h) to ensure compliance with select agent regulations.

As stated in the draft report, the objective of the review was to determine whether (b)(3) 42 USC 262 (b)(3) 42 USC 262 complies with Federal select agent regulations. The draft report identified two findings for which recommendations were made. (b)(3) 42 USC 262 (b)(3) 42 USC 262 has addressed these recommendations and made changes to their select agent program procedures. Below are OIG's recommendations as well as details on the corrective measures taken by (b)(3) 42 USC 262 (b)(3) 42 USC 262

Office of the Inspector General (OIG) Recommendation #1: Ensure that training is provided to all individuals before granting them access to select agent areas.

(b)(3) 42 USC 262a(h) (b)(3) 42 USC 262a(h) concurs with this finding and has instituted the following training procedures to ensure adherence to regulations 42 CFR Part 73.15 (a), 7 CFR Part 331.15 (a), and 9 CFR Part 121.15 (a):

1) Developed select agent training course - A select agent training course has been developed which examines all select agent regulatory requirements contained in 42 CFR Part 73, 7 CFR Part 331, 9 CFR Part 121 and includes the review of other pertinent regulations and guidelines. This training communicates site-specific information explaining how select agent regulations are followed at (b)(3) 42 USC 262. Beginning in January 2009, the new select agent training has been consistently administered to individuals beginning employment and when requesting access to select agents at (b)(3) 42 USC 262 and is required before access to any select agent or select agent registered

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Page 2 - Joseph E. Vengrin

area at 42 USC 26 is granted. Additionally, individuals are required to read the laboratory site-specific Biosafety Plan, the Biosecurity Plan, and the Incident Response Plan, as well as other pertinent materials. Individuals are evaluated by use of a written exam administered by the Responsible Official (RO). In addition to written exams, individuals are evaluated by their supervisors.

2) Required annual training - Traditionally, annual training has been conducted at 42 USC 26 during the period of October to December for all Security Risk Assessment (SRA)-approved individuals; however, as of January 2009, select agent training is now administered by the RO during an individual's birth month along with other annual requirements such as respirator fit testing and safety evaluations. The select agent annual training program requirements include a complete review of all manuals and plans which are documented by use of a manual review log. This log is signed by a supervisor or a peer who verifies that an individual understands the material. In addition, a series of review slides highlighting recent changes to the training program as well as frequently asked questions are provided by the RO. Upon completion of the training program a written exam is administered and evaluated by the RO prior to the individual receiving access to select agents and/or access to select agent areas.

3) Developed approval form - Access to select agent areas at 42 USC 26 is granted by use of the *Select Agent Access Form*. On this approval form, individuals request access to specific designated select agent areas. The form requires signatures from both the applicant and their supervisor. Following supervisory approval the form requires RO approval. The RO verifies an individual's SRA approval and ensures that the applicant has completed their required select agent training. In addition, the RO ensures that the requested access is consistent with the entity registration documents for the Principal Investigator. If an individual is delinquent on training or SRA approval, access is denied until these requirements are fulfilled.

Once all the required elements on the approval are completed, the approval form is forwarded to security personnel who assign appropriate accesses. A final review of all procedures is performed by a physical security specialist. In addition to obtaining training and approval for access to select agents and areas that house select agents, all (b)(3) 42 USC 262a(h) employees must annually meet safety requirements such as respirator fit testing, risk assessment of their duties, and evaluation of required immunizations.

With strict adherence to the processes outlined above, the (b)(3) 42 USC 262a(h) will maintain compliance with the training requirements as stated in 42 CFR Part 73.15 (a), 7 CFR Part 331.15(a), and 9 CFR Part 121.15(a).

Office of the Inspector General (OIG) Recommendation #2: Ensure that electronic access cards are coded in compliance with the (b)(3) 42 USC 262a(h) security plan.

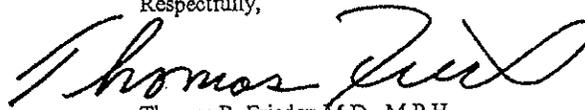
(b)(3) 42 USC 262a(h) concurs with this OIG finding and has instituted the following safeguards to address this recommendation:

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Page 4 - Joseph E. Vengrin

consideration of the comments contained in this memo and the technical comments as you develop the final report. We are happy to discuss any of these comments with you. Please direct any questions regarding these comments to Mr. Shaun Ratliff by telephone at (404) 639-2809 or by e-mail at iggao@cdc.gov.

Respectfully,



Thomas R. Frieden M.D., M.P.H.
Director, CDC, and
Administrator, Agency for Toxic
Substance and Disease Registry

Attachment

Office of Inspector General note: We have removed CDC's technical comments from this Appendix.

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DEC 17 2010

TO: Thomas R. Frieden, M.D., M.P.H.
Director
Centers for Disease Control and Prevention

FROM: George M. Reeb 
Acting Deputy Inspector General for Audit Services

SUBJECT: Review of the Centers for Disease Control and Prevention's (b)(3) 42 USC 262a(n) (b)(3) 42 USC 262a(n) With Select Agent Regulations (A-04-08-01056)

The attached final report provides the results of our review of the Centers for Disease Control and Prevention's (b)(3) 42 USC 262a(n) compliance with select agent regulations. This review is one of six reviews of Federal (b)(3) 42 USC 262a(n) compliance with select agent regulations.

This report contains restricted, sensitive information that may be exempt from release under the Freedom of Information Act, 5 U.S.C. § 552. The report will not be posted on the Internet. If information in the report is released pursuant to a request under the Act, the restricted, sensitive information and other information exempt from release will be redacted.

If you have any questions or comments about this report, please do not hesitate to call me, or your staff may contact Lori S. Pilcher, Assistant Inspector General for Grants, Internal Activities, and Information Technology Audits, at (202) 619-1175 or through email at Lori.Pilcher@oig.hhs.gov. We look forward to receiving your final management decision within 6 months. Please refer to report number A-04-08-01056 in all correspondence.

Attachment

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Department of Health & Human Services

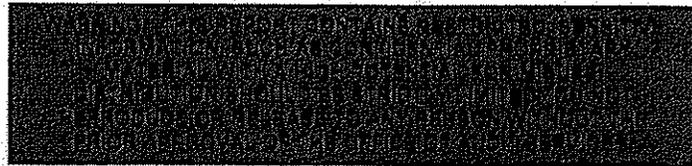
**OFFICE OF
INSPECTOR GENERAL**

**REVIEW OF THE CENTERS FOR
DISEASE CONTROL AND
PREVENTION'S**

(b)(5) 42 USC 262a(n)

(b)(3) 42 USC 262a(n)

**COMPLIANCE WITH SELECT
AGENT REGULATIONS**



Daniel R. Levinson
Inspector General

December 2010
A-04-08-01056

Office of Inspector General

<http://oig.hhs.gov>

The mission of the Office of Inspector General (OIG), as mandated by Public Law 95-452, as amended, is to protect the integrity of the Department of Health & Human Services (HHS) programs, as well as the health and welfare of beneficiaries served by those programs. This statutory mission is carried out through a nationwide network of audits, investigations, and inspections conducted by the following operating components:

Office of Audit Services

The Office of Audit Services (OAS) provides auditing services for HHS, either by conducting audits with its own audit resources or by overseeing audit work done by others. Audits examine the performance of HHS programs and/or its grantees and contractors in carrying out their respective responsibilities and are intended to provide independent assessments of HHS programs and operations. These assessments help reduce waste, abuse, and mismanagement and promote economy and efficiency throughout HHS.

Office of Evaluation and Inspections

The Office of Evaluation and Inspections (OEI) conducts national evaluations to provide HHS, Congress, and the public with timely, useful, and reliable information on significant issues. These evaluations focus on preventing fraud, waste, or abuse and promoting economy, efficiency, and effectiveness of departmental programs. To promote impact, OEI reports also present practical recommendations for improving program operations.

Office of Investigations

The Office of Investigations (OI) conducts criminal, civil, and administrative investigations of fraud and misconduct related to HHS programs, operations, and beneficiaries. With investigators working in all 50 States and the District of Columbia, OI utilizes its resources by actively coordinating with the Department of Justice and other Federal, State, and local law enforcement authorities. The investigative efforts of OI often lead to criminal convictions, administrative sanctions, and/or civil monetary penalties.

Office of Counsel to the Inspector General

The Office of Counsel to the Inspector General (OCIG) provides general legal services to OIG, rendering advice and opinions on HHS programs and operations and providing all legal support for OIG's internal operations. OCIG represents OIG in all civil and administrative fraud and abuse cases involving HHS programs, including False Claims Act, program exclusion, and civil monetary penalty cases. In connection with these cases, OCIG also negotiates and monitors corporate integrity agreements. OCIG renders advisory opinions, issues compliance program guidance, publishes fraud alerts, and provides other guidance to the health care industry concerning the anti-kickback statute and other OIG enforcement authorities.

Notices

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This report should not be reproduced or released to any other party without specific written approval from OAS.

OFFICE OF AUDIT SERVICES FINDINGS AND OPINIONS

The designation of financial or management practices as questionable, a recommendation for the disallowance of costs incurred or claimed, and any other conclusions and recommendations in this report represent the findings and opinions of OAS. Authorized officials of the HHS operating divisions will make final determination on these matters.

EXECUTIVE SUMMARY

BACKGROUND

The Public Health Security and Bioterrorism Preparedness and Response Act of 2002, 42 U.S.C. § 262a, requires the Department of Health & Human Services (HHS) to regulate select agents, which are biological materials that have the potential to pose a severe threat to public health and safety. Within HHS, this responsibility has been assigned to the Centers for Disease Control and Prevention (CDC), Division of Select Agents and Toxins (DSAT). In collaboration with the U.S. Department of Agriculture, CDC establishes select agent regulations and monitors and enforces compliance with the regulations.

Any government agency (Federal, State, or local), academic institution, research organization, or other legal entity that possesses, uses, or transfers select agents must register with CDC and comply with Federal select agent regulations. (We refer collectively to these organizations as “entities.”) Entities must, among other things, appoint a Responsible Official to ensure compliance with the regulations; restrict access to select agents to individuals approved by the HHS Secretary based on a security risk assessment by the Attorney General (referred to as “approved individuals”); develop and implement security, biosafety, and incident response plans; provide training on biosafety and security; maintain detailed select agent inventory and access records; and comply with select agent transfer requirements.

Following the 2001 terrorist attacks and anthrax release, we conducted a series of reviews of compliance with Federal select agent regulations by State, local, nonprofit, and university laboratories. In April 2008, we began a series of similar reviews at six Federal entities. This review, one in the series, addresses compliance by CDC’s (b)(5)-42 USC 262a(h)

(b)(5)-42 USC 262a(h)

OBJECTIVE

Our objective was to determine whether (b)(5)-42 USC 262a(h) complied with Federal select agent regulations.

SUMMARY OF FINDINGS

(b)(5)-42 USC 262a(h) complied with some Federal select agent regulations. Specifically, (b)(5)-42 USC 262a(h) had appointed a Responsible Official and developed and implemented an incident response plan. However, (b)(5)-42 USC 262a(h) did not always:

- ensure the physical security of select agents or restrict access to select agents to approved individuals,
- ensure that individuals received select agent training,

- maintain required inventory records or ensure that select agent inventory was stored only in registered areas, or
- obtain DSAT approval to transfer select agents or ensure that only approved individuals accepted delivery of select agents.

These weaknesses could have compromised 3142 USC 262a ability to safeguard select agents from accidental or intentional loss and to ensure the safety of individuals who work with select agents.

RECOMMENDATIONS

We recommend that 3142 USC 262a

- follow its security plan requirements regarding physical security measures,
- ensure that only approved individuals are allowed access to select agent areas,
- ensure that all required training is provided to approved individuals,
- ensure that inventory records describe the precise location of all select agents and that select agents are stored only in areas listed on the certificate of registration, and
- include in its biosafety plan a requirement to confirm that materials are inactive before transferring them without authorization.

CENTERS FOR DISEASE CONTROL AND PREVENTION COMMENTS AND OFFICE OF INSPECTOR GENERAL RESPONSE

In comments on our draft report, CDC concurred in principle with our recommendations and provided detailed information on its current and planned security measures. CDC did not concur with some of our findings. CDC also submitted technical comments, which we addressed as appropriate. The complete text of CDC's comments is included as Appendix B.

In response to CDC's comments, we revised three findings and one recommendation.

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B: CENTERS FOR DISEASE CONTROL AND PREVENTION COMMENTS

INTRODUCTION

BACKGROUND

The Public Health Security and Bioterrorism Preparedness and Response Act of 2002, 42 U.S.C. § 262a, requires the Department of Health & Human Services (HHS) to regulate select agents, which are biological materials that have the potential to pose a severe threat to public health and safety.¹ Within HHS, this responsibility has been assigned to the Centers for Disease Control and Prevention (CDC), Division of Select Agents and Toxins (DSAT). In collaboration with the U.S. Department of Agriculture (USDA), CDC establishes select agent regulations and monitors and enforces compliance with the regulations.²

Any government agency (Federal, State, or local), academic institution, research organization, or other legal entity that possesses, uses, or transfers select agents must register with CDC and comply with Federal select agent regulations. (We refer collectively to these organizations as “entities.”)

Federal Select Agent Regulations

Federal select agent regulations (42 CFR part 73) require that entities, among other things, appoint a Responsible Official to ensure compliance with the regulations; restrict access to select agents to individuals approved by the HHS Secretary based on a security risk assessment by the Attorney General (referred to as “approved individuals”); develop and implement security, biosafety, and incident response plans; provide training on biosafety and security; maintain detailed select agent inventory and access records; and comply with select agent transfer requirements. Appendix A contains the specific Federal regulations relevant to this review.

(b)(3) 42 USC 262a(n)

¹ For purposes of this report, “select agents” refers to all agents and toxins listed in 42 CFR §§ 73.3 and 73.4.

² CDC regulates select agents that could pose a severe threat to public health and safety. USDA’s Animal and Plant Health Inspection Service (APHIS) regulates select agents and toxins that could pose a severe threat to animal or plant health. CDC and APHIS coordinate regulatory activities for those agents that affect both humans and animals (known as overlap select agents and toxins).

Office of Inspector General Reviews

Following the 2001 terrorist attacks and anthrax release, we conducted a series of reviews of compliance with Federal select agent regulations by State, local, nonprofit, and university laboratories. In April 2008, we began a series of similar reviews at six Federal entities. This review is one in the series.

In addition, in a prior review, we determined whether only approved individuals accessed select agents transferred to and from (b)(3) 42 USC 262a(h)

(b)(3) 42 USC 262a(h)

OBJECTIVE, SCOPE, AND METHODOLOGY

Objective

Our objective was to determine whether (b)(3) 42 USC 262a(h) complied with Federal select agent regulations.

Scope

Our review covered the period April 18, 2005, the effective date of HHS's final rule for implementing select agent regulations,⁵ through April 2009. We did not perform an indepth review of (b)(3) 42 USC 262a(h) internal control structure. Rather, we limited our review to controls related to (b)(3) 42 USC 262a(h) compliance with select agent regulations.

We performed our fieldwork at (b)(3) 42 USC 262a(h)

(b)(3) 42 USC 262a(h)

⁵ 70 Fed. Reg. 13294–13325 (Mar. 18, 2005).

Methodology

To accomplish our objective, we:

- reviewed applicable Federal laws, regulations, and guidance;
- reviewed CDC records related to (b) (6), (b) (7)(C) registration;
- reviewed (b) (6), (b) (7)(C) select agent security plan, biosafety plan, and incident response plan;
- held discussions with (b) (6), (b) (7)(C) and DSAT officials to gain an understanding of policies and procedures for implementing select agent regulations;
- tested (b) (6), (b) (7)(C) security, biosafety, and incident response procedures;
- reviewed (b) (6), (b) (7)(C) records related to biosafety and security training provided to a judgmentally selected sample of 30 approved individuals;
- reviewed (b) (6), (b) (7)(C) select agent inventory and access records; and
- reviewed (b) (6), (b) (7)(C) procedures for transferring select agents.

We conducted this performance audit in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objective.

FINDINGS AND RECOMMENDATIONS

(b) (6), (b) (7)(C) complied with some Federal select agent regulations. Specifically, (b) (6), (b) (7)(C) had appointed a Responsible Official and developed and implemented an incident response plan. However, (b) (6), (b) (7)(C) did not always:

- ensure the physical security of select agents or restrict access to select agents to approved individuals,
- ensure that individuals received select agent training,
- maintain required inventory records or ensure that select agent inventory was stored only in registered areas, or

- obtain DSAT approval to transfer select agents or ensure that only approved individuals accepted delivery of select agents.

These weaknesses could have compromised (b) (3) 42 USC 262a ability to safeguard select agents from accidental or intentional loss and to ensure the safety of individuals who work with select agents.

SELECT AGENT ACCESS

Pursuant to 42 CFR § 73.11(a), entities must develop and implement a written security plan to safeguard select agents against unauthorized access, theft, loss, or release. Further, 42 CFR § 73.11(c)(5) states: “The security plan must ... [d]escribe ... protocols for changing access numbers or locks following staff changes”

Pursuant to 42 CFR § 73.10(a), entities may authorize access to select agents only to approved individuals.⁶ In addition, 42 CFR § 73.10(j) states that the Responsible Official must immediately notify CDC when an individual’s access to select agents is terminated and the reasons for the termination.

Physical Security of Select Agents

(b) (3) 42 USC 262a(h)

(b) (3) 42 USC 262 did not fully adhere to its security plan requirements. Specifically:

-
-

(b) (3) 42 USC 262a(h)

⁶ Pursuant to 42 CFR § 73.11(d)(2), an entity may allow an unapproved individual to conduct routine cleaning, maintenance, repairs, or other activities not related to select agents if the individual is continuously escorted by an approved individual.

(b) (3) 42 USC 262a(h)

(b)(3) 42 USC 262a(h)

Approved Individuals

According to (b)(3) 42 USC 262a security plan, individuals awaiting notification of approval by the HHS Secretary were allowed to access select agent laboratory and storage areas only if escorted by an approved individual. (b)(3) 42 USC 262a(h)

(b)(3) 42 USC 262a(h)

SELECT AGENT TRAINING

Pursuant to 42 CFR § 73.15(a), entities must provide biosafety and security training to individuals before they access select agent areas. In addition, 42 CFR § 73.15(b) states that entities must provide annual refresher training to approved individuals.

We could not verify that 10 of 30 sampled approved individuals had received the required training. For three individuals, there was no documentation that they had received any training. For seven individuals, there was no documentation that they had received annual refresher training.

SELECT AGENT INVENTORY

Pursuant to 42 CFR § 73.17(a)(1), entities must maintain an accurate, current inventory, which includes information showing where each select agent is stored (e.g., building, room, and freezer). In addition, pursuant to 42 CFR § 73.7(g), entities must have a valid certificate of registration for one physical location (a building, a room, or a group of buildings) for select agents.

Incomplete Inventory Records

Not all select agent inventory records at (b)(3) 42 USC 262a contained the building number, room number, freezer number, or other information required by regulations. (b)(3) 42 USC 262a security plan did not require that these records fully describe the precise storage location of the select agents. The plan stated: "The inventory record does not need to fully describe the location; for example, the rack/box/vial number may be specified explicitly, but the building/floor/room/freezer information may be the same for all, understood by the accountable scientist, and omitted from the record." After our fieldwork, (b)(3) 42 USC 262a officials advised us that (b)(3) 42 USC 262a had revised its security plan to require that inventory records fully describe the storage location of select agents.

Agents Stored in Areas Not Listed in (b)(3) 42 USC 262a Registration

(b)(3) 42 USC 262 stored some select agents in areas not listed in its registration. (b)(3) 42 USC 262a(h)

(b)(3) 42 USC 262a(h)

(b)(3) 42 USC 262a(h)

SELECT AGENT TRANSFERS

Pursuant to 42 CFR § 73.7(a), “[u]nless exempted under § 73.5, an individual or entity shall not possess, use, or transfer any HHS select agent or toxin without a certificate of registration issued by the HHS Secretary. Unless exempted under § 73.6 or 9 CFR part 121.6, an individual or entity shall not possess, use, or transfer overlap select agents or toxins, without a certificate of registration issued by the HHS Secretary and Administrator [of APHIS].” Furthermore, 42 CFR § 73.16(a) states: “... a select agent or toxin may only be transferred to individuals or entities registered to possess, use, or transfer that agent or toxin. A select agent or toxin may only be transferred under the conditions of this section and must be authorized by CDC or APHIS prior to the transfer.” Additionally, pursuant to 42 CFR § 73.10(a), entities may authorize access to select agents only to approved individuals.

Unauthorized Transfers

On two occasions in 2006, (b)(3) 42 USC 262a(m) without authorization to do so.¹² In late March 2006, (b)(3) 42 USC 262a(h)

(b)(3) 42 USC 262a(h)

(b)(3) 42 USC 262a(h)

(b)(3) 42 USC 262a(h)

Packages Received by Unapproved Individuals

During our audit period, six unapproved individuals—five individuals from (b)(3) 42 USC 262a delivery contractor and one security guard—received and signed for packages containing select agents transferred to (b)(3) 42 USC 262a(h)

(b)(3) 42 USC 262a(h)

RECOMMENDATIONS

We recommend that (b)(3) 42 USC 262a

- follow its security plan requirements regarding physical security measures,
- ensure that only approved individuals are allowed access to select agent areas,
- ensure that all required training is provided to approved individuals,

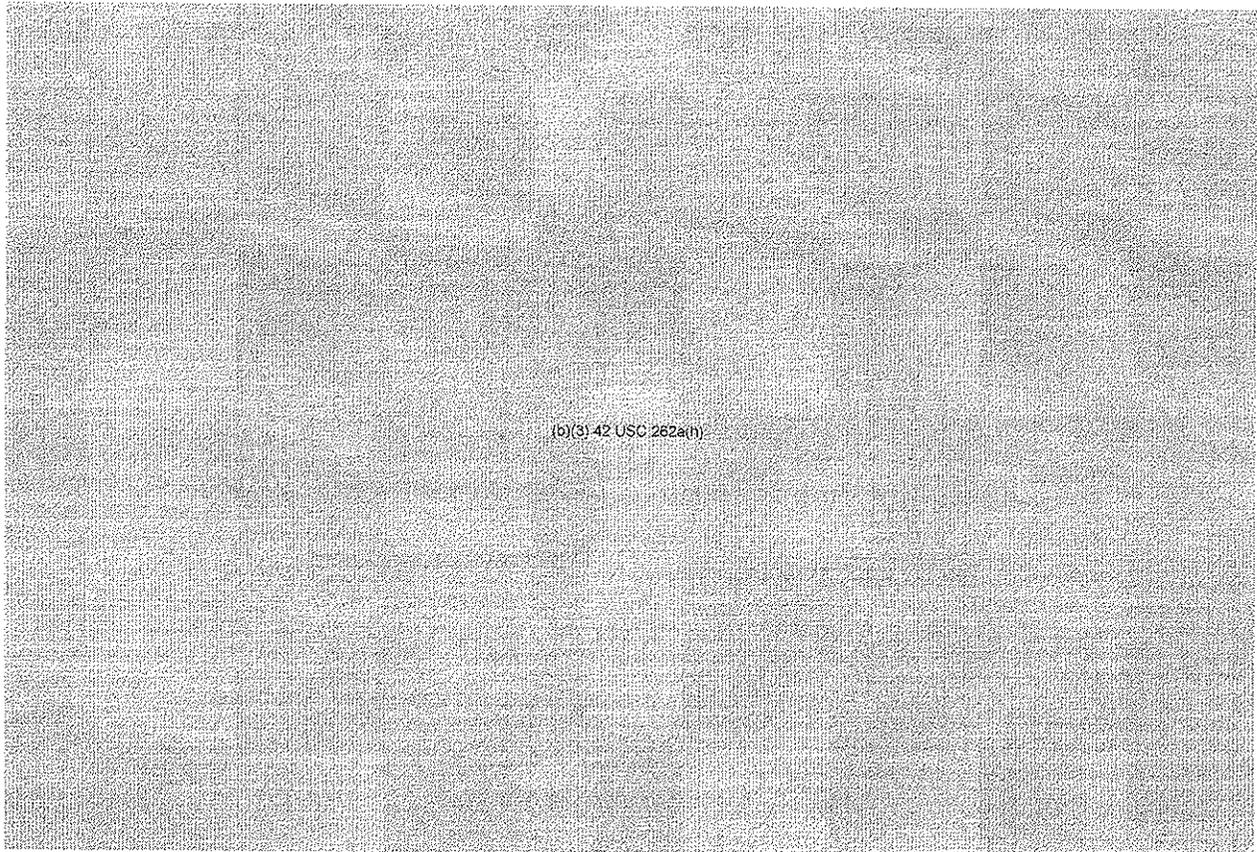
(b)(3) 42 USC 262a(h)

- ensure that inventory records describe the precise location of all select agents and that select agents are stored only in areas listed on the certificate of registration, and
- include in its biosafety plan a requirement to confirm that materials are inactive before transferring them without authorization.

CENTERS FOR DISEASE CONTROL AND PREVENTION COMMENTS AND OFFICE OF INSPECTOR GENERAL RESPONSE

In comments on our draft report, CDC concurred in principle with our recommendations and provided detailed information on its current and planned security measures. CDC did not concur with some of our findings. CDC's comments on those findings and our responses are summarized below. CDC also submitted technical comments, which we addressed as appropriate. The complete text of CDC's comments is included as Appendix B.

In response to CDC's comments, we revised three findings and one recommendation.



APPENDIXES

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APPENDIX A: FEDERAL SELECT AGENT REGULATIONS

- Regulations (42 CFR §§ 73.3 and 73.4) list select agents and toxins, which are biological materials that have the potential to pose a severe threat to public health and safety (referred to as “select agents” for purposes of the report and this Appendix).
- Regulations (42 CFR § 73.7(a)) require that an individual or entity not possess, use, or transfer select agents without a certificate of registration issued by the Secretary of the U.S. Department of Health & Human Services (HHS).
- Regulations (42 CFR § 73.7(b)) require each entity to designate an individual to be its Responsible Official.
- Regulations (42 CFR § 73.7(g)) require entities to have a valid certificate of registration for one physical location (a building, a room, or a group of buildings) for select agents.
- Regulations (42 CFR § 73.7(h)) require an entity to amend its registration to reflect changes in circumstances (personnel changes, changes in the activities involving any select agent, or the addition or removal of select agents).
- Regulations (42 CFR § 73.9(a)) require that the Responsible Official have the authority and responsibility to act on behalf of the entity and ensure the entity’s compliance with requirements of the select agent regulations.
- Regulations (42 CFR § 73.10(a)) require an entity to authorize access to select agents only to individuals approved by the HHS Secretary following a security risk assessment by the Attorney General (referred to as “approved individuals”).
- Regulations (42 CFR § 73.10(j)) require the Responsible Official to immediately notify the Centers for Disease Control and Prevention (CDC) (or the U.S. Department of Agriculture) when an individual’s access to select agents is terminated and the reasons for the termination.
- Regulations (42 CFR § 73.11(a)) require entities to develop and implement a written security plan. The security plan must be sufficient to safeguard select agents against unauthorized access, theft, loss, or release.
- Regulations (42 CFR § 73.11(b)) require that the entity’s security plan be designed according to a site-specific risk assessment and provide protection in accordance with the risk of the select agent, given its intended use.
- Regulations (42 CFR § 73.11(c)) require the entity’s security plan to contain procedures for physical security, inventory control, and information systems control, as well as provisions for controlling access to select agents. In addition, each entity’s plan must contain provisions for routine cleaning, maintenance, and repairs and procedures for removing

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unauthorized or suspicious persons. Each plan must describe procedures for addressing the loss or compromise of keys, passwords, or combinations and protocols for changing access numbers or locks following staff changes. Plans also must contain procedures for reporting unauthorized or suspicious persons or activities; the loss, theft, or release of select agents; or the alteration of inventory records, as well as procedures for ensuring that all approved individuals understand and comply with security procedures.

- Regulations (42 CFR § 73.11(d)) require entities to allow access to select agents only to approved individuals. However, unapproved individuals who conduct routine cleaning, maintenance, repairs, or other activities not related to select agents may access select agent areas only when continuously escorted by an approved individual. In addition, freezers, refrigerators, cabinets, and other containers where select agents are stored are required to be secured against unauthorized access. The security plan also must contain procedures for intraentity transfers of select agents, the avoidance of sharing individuals' unique means of access to select agents, and the separation of select agent areas from public areas.
- Regulations (42 CFR § 73.11(f)) require entities to review annually and revise, as necessary, their security plan. Further, entities must conduct drills or exercises at least annually to test and evaluate the effectiveness of their plan. The plan must be reviewed and revised, as necessary, after any drill or exercise and after any incident.
- Regulations (42 CFR § 73.12(a)) require entities to develop and implement a written biosafety plan that is commensurate with the risk of the agent, given its intended use. The biosafety plan must contain sufficient information and documentation to describe the biosafety and containment procedures.
- Regulations (42 CFR § 73.12(d)) require entities to review annually and revise, as necessary, their biosafety plan. Further, entities must conduct drills or exercises at least annually to test and evaluate the effectiveness of their plan. The plan must be reviewed and revised, as necessary, after any drill or exercise and after any incident.
- Regulations (42 CFR § 73.14(a)) require entities to develop and implement a written incident response plan. The incident response plan must be coordinated with any entitywide plans, kept in the workplace, and available to employees for review.
- Regulations (42 CFR § 73.14(c)) require each entity's incident response plan to contain information related to names and contact information for responsible entity and building officials, personnel roles and lines of authority and communication, planning and coordination with local emergency responders, procedures for employees performing rescue or medical duties, a list of personal protective and emergency equipment, site security and control, procedures for emergency evacuation, and decontamination procedures.
- Regulations (42 CFR § 73.14(d)) require entities to review and revise, as necessary, their incident response plans. Further, entities must conduct drills or exercises at least annually to

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test and evaluate the effectiveness of their plan. The plan must be reviewed and revised, as necessary, after any drill or exercise and after any incident.

- Regulations (42 CFR § 73.15(a)) require entities to provide information and training on biosafety and security to individuals before they access select agent areas.
- Regulations (42 CFR § 73.15(b)) require entities to provide annual refresher training for approved individuals.
- Regulations (42 CFR § 73.15(c)) require entities to maintain a record of training provided to each individual. The record must include the name of the individual, the date of the training, a description of the training, and the means used to verify that the employee understood the training.
- Regulations (42 CFR § 73.16) require entities to transfer a select agent only to an entity registered to possess that particular select agent. Each transfer must be authorized by CDC (or the U.S. Department of Agriculture) before the transfer. In addition, the sender must comply with all laws concerning packaging and shipping.
- Regulations (42 CFR §§ 73.17(a)(1) and 73.17(a)(2)) require entities to maintain complete records relating to select agent inventories.
- Regulations (42 CFR § 73.17(a)(3)) require entities to maintain a current list of all approved individuals.
- Regulations (42 CFR § 73.17(a)(4)) require entities to maintain complete records related to all entries into areas containing select agents, including the name of the individual, name of the escort (if applicable), and date and time of entry.
- Regulations (42 CFR § 73.17(b)) require entities to implement a system to ensure that all records and databases created under 42 CFR part 73 are accurate, that access to them is controlled, and that their authenticity may be verified.

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APPENDIX B: CENTERS FOR DISEASE CONTROL AND PREVENTION COMMENTS



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control
and Prevention (CDC)
Atlanta GA 30333

JUL 23 2010

TO: Daniel R. Levinson
Inspector General
Department of Health and Human Services (HHS)

FROM: Director
Centers for Disease Control and Prevention

SUBJECT: Office of Inspector General's Draft Report: "Review of the Centers for Disease Control and Prevention's (b)(3) (42 USC 262a) Compliance With Select Agent Regulations" June 23, 2010 (A-04-08-01056)

The Centers for Disease Control and Prevention (CDC), Office of Surveillance, Epidemiology, and Laboratory Services (OSELs) and the Office of Security and Emergency Preparedness (OSEP) appreciate the opportunity to review and provide comments on the Office of Inspector General's draft report, "Review of the Centers for Disease Control and Prevention's (b)(3) (42 USC 262a) Compliance with Select Agent Regulations" (A-04-08-01056). Thank you for your review of this important issue.

OBJECTIVE

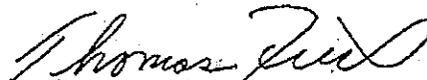
As stated in the draft, the objective of this review was to determine whether (b)(3) (42 USC 262a) complied with Federal select agent regulations. The draft identified five findings regarding the CDC (b)(3) (42 USC 262a) Laboratory's compliance with select agent regulations.

SUMMARY OF FINDINGS

The draft provided a summary of findings (Page i) that stated that (b)(3) (42 USC 262a) complied with some Federal select agent regulations in that, specifically, (b)(3) (42 USC 262a) had appointed a Responsible Official and had developed and implemented an incident response plan. The draft summary of findings further indicated that (b)(3) (42 USC 262a) did not always: 1) ensure the physical security of select agents or restrict access to select agents to approved individuals; 2) ensure that individuals received select agent training; 3) maintain required inventory records or ensure that select agent inventory was stored only in registered areas; 4) or obtain DSAT approval to transfer select agents or ensure that only approved individuals accepted delivery of select agents. The summary of findings also stated that these weaknesses could have compromised (b)(3) (42 USC 262a) ability to safeguard select agents from unintentional or intentional loss and to ensure the safety of individuals who work with select agents.

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General and specific technical comments are attached to the CDC (b) (5) 42 USC 262a(h) response to the OIG, "Review of the Centers for Disease Control and Prevention's (b) (5) 42 USC 262a(h) Compliance With Select Agent Regulations" (A-04-08-01056) dated June 23, 2010. While the CDC generally concurs in principle with findings in the report, there are several areas we would like to clarify and reiterate that policies and procedures are already in place after we self reported many of the finding indicated in the OIG report. The additional clarification is provided in the attached general and specific technical comments.


Thomas R. Frieden, M.D., M.P.H.
Director

Attachments: General Comments and Specific Technical Comments

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Page 7 and Page 8, RECOMMENDATIONS

The first word in each bulleted item should appear in upper case type.

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U.S. Department of Agriculture



Office of Inspector General
Southeast Region

Audit Report

Animal and Plant Health Inspection Service Evaluation of the Implementation of the Select Agent or Toxin Regulations Phase II

Report No. 33601-3-AT
January 2006



UNITED STATES DEPARTMENT OF AGRICULTURE

OFFICE OF INSPECTOR GENERAL

Washington, D.C. 20250



January 17, 2006

REPLY TO

ATTN OF: 33601-3-At

TO: W. Ron DeHaven
Administrator
Animal and Plant Health Inspection Service

ATTN: William J. Hudnall
Deputy Administrator for Marketing Regulatory Program
Business Services

FROM: Robert W. Young /S/
Assistant Inspector General
for Audit

SUBJECT: Evaluation of the Implementation of the Select Agent or Toxin
Regulations (Phase II)

This report presents the results of the subject audit. Your response to the report, dated December 2, 2005, is included as exhibit A, with excerpts and the Office of Inspector General's (OIG) position incorporated into the Findings and Recommendations section of the report.

Based on your response, we have reached management decisions on Recommendations 2, 3, and 10. To achieve management decisions on Recommendations 1, 4, 5, 6, 7, 8, 9, 11, 12, and 13, we need additional corrective actions as outlined in the OIG Position section of the report, following each recommendation.

In accordance with Departmental Regulation 1720-1, please furnish a reply within 60 days describing the corrective actions taken or planned and the timeframes for implementation of those recommendations for which management decisions have not yet been reached. Please note that the regulation requires that management decisions be reached on all recommendations within a maximum of 6 months from report issuance.

We appreciate the courtesies and cooperation extended to us by members of your staff during the audit.

Executive Summary

Animal and Plant Health Inspection Service Evaluation of the Implementation of the Select Agent or Toxin Regulations Phase II, Audit Report No. 33601-3-At

Results in Brief

After the events of September 11, 2001, the Government has taken a number of steps to strengthen homeland security. The Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (Public Law 107-188, signed June 12, 2002), included provisions for enhancing controls over dangerous biological agents and toxins. The Act addressed the lack of authority for the Secretary of Agriculture to regulate possession of biological agents that, through acts of bioterrorism, could have a devastating impact on the domestic agricultural economy.¹ With passage of the Act, the Secretary of Agriculture was required to promulgate regulations to provide for the establishment and enforcement of standards and procedures governing the possession, use, and transfer of select agents or toxins, including security measures and controls to limit access to only those individuals that have a legitimate need to handle or use such agents or toxins. The Animal and Plant Health Inspection Service (APHIS) was delegated authority to administer the regulations for the U.S. Department of Agriculture.

The objective of the audit was to evaluate APHIS' implementation of regulations governing the possession, use, and transfer of biological agents and toxins. The audit was conducted in two phases. In Phase I (Audit No. 33601-2-At), we evaluated the agency's overall implementation of the regulations governing the possession, use, and transfer of biological agents and toxins. In Phase II, we made field visits to locations where select agents or toxins are used or stored to determine whether controls are in place and functioning as designed by examining registered entities' compliance with the regulations. This report presents the results of Phase II of our review.

We found that APHIS' oversight and enforcement of regulations regarding the security over select agents or toxins needed strengthening. As we reported in Phase I of our review,² the agency had not fully implemented controls for enforcing safeguard and security measures to prevent access to dangerous biological agents and toxins, as required by legislation. During our fieldwork in Phase II, we found that APHIS had not ensured that entities were: fully complying with regulations regarding security plans; restricting access to select agents or toxins; training individuals authorized to possess, use, or transfer select agents or toxins; and maintaining current and accurate inventories. These weaknesses occurred because APHIS had not performed timely or adequate reviews to ensure that security measures were implemented in accordance with the regulatory requirements. As we reported in Phase I, APHIS initially

¹ House of Representatives Conference Report No. 107-481, dated May 21, 2002.

² Audit Report No. 33601-2-At, issued June 23, 2005.

reviewed registration applications only to ensure that a security plan was submitted before granting provisional registrations. The agency did not determine the adequacy of the plans. In Phase I, we also reported that APHIS' inspections of the entities were not thorough enough to determine whether security was adequate. As a result, select agents or toxins were vulnerable to potential theft or misuse.

We found that APHIS had not updated its list of individuals authorized to access select agents or toxins. On October 8, 2004, APHIS provided us a current list of approved individuals granted access to select agents or toxins (authorized list). However, we found that the APHIS list did not always agree with the lists maintained by the registered entities. We found that 5 of the 10 entities reviewed had lists that were different from APHIS'. The differences occurred because (1) APHIS did not update the lists when notified by the entities that certain individuals no longer had access to the select agents or toxins or (2) the entities did not notify APHIS of individuals no longer having access. As a result, APHIS does not have accurate information to use in monitoring registered entities' compliance with requirements for restricting access to the select agents.

APHIS had not adequately safeguarded sensitive security and personal information pertaining to individuals authorized access to possess, use, or transfer select agents or toxins. We identified two instances where information regarding authorized individuals was provided to the wrong registered entity. This occurred because of human error, which we attributed in part to the fact that APHIS had not developed a national database of registered entities. This database should contain critical information including the names of individuals authorized to access select agents at the particular entity.³ Until the national database is developed, APHIS will have to continue to rely on a mix of manual records and computerized spreadsheets maintained separately while administering the select agent program. In addition, APHIS had not established internal controls, in the form of policies and procedures, to prevent such occurrences. As a result, there is a greater risk that sensitive information is inadvertently disclosed in violation of the Act.

For our Phase I review, we reported that APHIS granted provisional registrations to entities without determining whether their security plans provided adequate safeguard and security measures. During our site visits in Phase II, we found that none of the 10 entities we reviewed had fully complied with the regulations. We selected 10 entities registered with APHIS, and performed site visits to test the entities' compliance with the regulations and to determine whether security controls were adequate and functioning. We found that security plans (1) were not based on site-specific risk assessments as required, (2) did not address critical requirements in the

³ This condition was identified in our Phase I report (Audit No. 33601-2-At).

regulations, and (3) were not performance tested or reviewed and updated annually by the registered entities.

Registered entities we visited expressed concerns regarding APHIS oversight, including inadequate guidance to implement the select agent rules, untimely review and response to required submissions, and insufficient timeframes for responding to APHIS inquiries. Inadequate guidance and untimely reviews of security plans may have contributed to some of the deficiencies we identified. However, we noted that, in many cases, deficiencies were due to the entities not following regulatory requirements. Even though each had been inspected by APHIS for compliance with the regulations prior to our review, we identified a number of security deficiencies at the sites visited.⁴ We found that registered entities:

1. did not adequately restrict access to select agents or toxins as required by the regulations;
2. did not maintain adequate inventories of select agents; and
3. did not maintain adequate documentation concerning Biocontainment or Biosafety and Security training.

For our Phase I review, we reported that APHIS had not established policies and procedures to ensure that inspections of the registering entities' security measures were consistent and thorough. Inspections performed by APHIS did not provide clear documentation concerning the nature or extent of deficiencies, and did not always conclude as to whether security measures implemented by the registered entities were adequate. We also reported that although some inspections revealed deficiencies, APHIS did not always notify the registered entities of the results of the inspections and address, in writing, the nature of the deficiencies or the requirements for followup.

Because the Act requires APHIS and the Center for Disease Control (CDC) to develop and implement procedures to share responsibilities for inspecting entities that handle overlap agents, we met with officials from the Health and Human Services (HHS) Office of Inspector General (OIG) to coordinate our recommendations. The HHS-OIG conducted reviews of entities registered with CDC and identified issues similar to those identified during our reviews of entities registered with APHIS.

Recommendations in Brief

We are recommending that APHIS re-inspect registered entities to ensure compliance with regulations regarding the security over select agents. The inspections should be done using formal written procedures to ensure consistent and thorough reviews. In developing policies and procedures for

⁴ Deficiencies were discussed with responsible officials at entities visited.

reviewing and inspecting entities' compliance with the regulations, APHIS should include steps to:

- ensure registered entities base their security plans on a site-specific risk analysis;
- verify that the entities' security plans have thoroughly addressed all critical areas identified by the regulations;
- verify that entities are conducting and documenting annual performance tests of their security plans, and are updating plans based on the results of the performance tests, drills, or exercises;
- compare its list of authorized individuals with the names of individuals having access to areas with select agents;
- identify and examine all areas where select agents are used or stored to ensure that access to those areas are properly secured;
- verify that the entities have established and implemented inventory controls and perform tests to see that inventories are accurate and up to date; and
- verify that the entities have provided annual training, including required security training, to all individuals authorized to access select agents, and have documented the training as required.

We are also recommending that APHIS develop and implement written policies and procedures to ensure authorized lists are accurately and promptly updated. The procedures should include periodically disseminating the lists to registered entities and requiring the entities to verify APHIS' records, and either provide corrections or attest to the accuracy of the list. Additionally, we are recommending that APHIS develop and implement internal controls designed to prevent the release of sensitive security information associated with registered entities.

Agency Response

APHIS provided a written response to the official draft report on December 2, 2005. We have incorporated applicable portions of the response into the Findings and Recommendations section of this report. The agency response is included as exhibit A.

OIG Position

Based on your response, we have reached management decisions on Recommendations 2, 3, and 10. To achieve management decisions on Recommendations 1, 4, 5, 6, 7, 8, 9, 11, 12, and 13, we need additional corrective actions as outlined in the OIG Position section of the report, following each recommendation.

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Background and Objectives

Background

Plant and animal biological agents and toxins are considered “select” agents if they appear on a list prepared by the U.S. Department of Agriculture (USDA), and published in the *Federal Register* in accordance with the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (Public Law 107-188) (the Act). The Agricultural Bioterrorism Protection Act of 2002⁵ provides for the regulation of those agents and toxins that have the potential to pose a severe threat to animal or plant health, or to animal or plant products.

The Act also provides for the regulation of biological agents and toxins listed as dangerous by the Department of Health and Human Services (HHS). Where both HHS and USDA list the same agents, known as overlap agents, the Act provides for interagency coordination between the two departments. The Centers for Disease Control and Prevention (CDC) has responsibility for enforcing the Act on behalf of HHS; the Animal and Plant Health Inspection Service (APHIS) has responsibility for enforcing the Act on behalf of USDA.

The Act also required USDA’s Secretary to establish:

- safety requirements for select agents, ensuring that appropriate skills exist to handle the agents and that proper laboratory facilities are available to contain and dispose of them;
- security requirements to prevent access to select agents for use in domestic or international terrorism or for any other criminal purpose; and
- requirements to protect animal and plant health, and animal and plant products in the event of a transfer of a select agent.

The Act requires all persons in possession of any select biological agent or toxin, including those select agents listed by CDC, to notify CDC or the Secretary of Agriculture of such possession. APHIS published the first list of select agents or toxins as an interim rule in the *Federal Register* in August 2002. The notification forms were due to APHIS no later than October 11, 2002.

APHIS published the final list of select agents or toxins on December 13, 2002. The list of plant agents appeared in 7 *Code of Federal Regulations* (CFR) 331 and the list of overlap and animal agents appeared in 9 CFR 121.

⁵ Title II, subtitle B, of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, is cited as the “Agricultural Bioterrorism Protection Act of 2002.”

Both regulations established safety, security, and transfer requirements for the select agents.

The Act required that APHIS publish an interim final rule for carrying out the safeguard and security measures within 180 days of passage of Public Law 107-188. The interim final rule, published on December 13, 2002, provided the regulations that registered entities were required to follow at the time of our site visits. The interim final rule became effective on February 11, 2003. Our review included an examination of the entities' compliance with the interim final rule. On March 18, 2005, APHIS adopted as a final rule, with changes, the interim final rule. The final rule promulgated regulations that became effective on April 18, 2005. The final rule provided clarification for issues such as inventory control requirements for select agents, and state that additional guidance will be forthcoming for issues such as security required for select agents or toxins.

One other requirement set forth by the Act (and repeated as regulation in the *Federal Register*) was that all entities possessing, using, or transferring select agents must register with the appropriate regulatory agency, APHIS or CDC. Entities with overlap agents could register with either agency. As part of the registration process, the entities' responsible official (RO), the alternate RO, the entity, and—where applicable—the individual who owns or controls the entity must undergo a security risk assessment by the Criminal Justice Information Services (CJIS) Division of the Federal Bureau of Investigation (FBI). Moreover, those individuals identified by an entity as having a legitimate need to handle or use select biological agents or toxins must undergo a security risk assessment by the CJIS Division.

To minimize the disruption of research and educational projects that were underway as of the effective date of the regulations (February 11, 2003), APHIS and CDC established a phase-in period that gave individuals and entities until November 12, 2003, to reach full compliance with the regulations. The phase-in dates were as follows:

- By March 12, 2003, the RO was to submit the registration application package to the regulatory agency. The official was also to transmit to the Attorney General the names of the RO, the entity, and the individual who owned the entity.
- By April 11, 2003, the RO was to submit to the Attorney General the names of all the individuals with the entity that had a legitimate need to use the select agents.
- By June 12, 2003, the RO was to submit to APHIS the security section of the entity's security plan.

- By September 12, 2003, the RO was to implement the security section of the entity's Biocontainment/Biosafety and Security Plan and provide security training in accordance with regulations.
- By November 12, 2003, the registration application process was to be complete and the entity in full compliance.

Objectives

The primary objective of this audit was to evaluate APHIS' implementation of regulations governing the possession, use, and transfer of biological agents and toxins. For this phase, we conducted field visits to locations where select agents or toxins are used or stored to determine whether established controls are functioning as designed by examining registered entities' compliance with the regulations, as well as assess APHIS' oversight of the entities.

Findings and Recommendations

Section 1: APHIS Controls Over the Select Agent Program

Finding 1

APHIS Did Not Ensure That Registered Entities Had Developed and Implemented Adequate Security Measures

APHIS had not ensured that entities were fully complying with regulations regarding the development and implementation of security plans; restricting access to select agents or toxins; training for individuals authorized to possess, use, or transfer select agents or toxins; and maintaining accurate inventories. This occurred because APHIS had not performed adequate or timely reviews to ensure that security measures were implemented in accordance with the regulatory requirements. As we reported in Phase I, APHIS initially reviewed registration applications only to ensure that a security plan was submitted before granting provisional registrations. The agency did not determine the adequacy of the plans. In Phase I, we also reported that APHIS' inspections of the entities were not thorough enough to determine whether security was adequate. As a result, select agents or toxins were vulnerable to potential theft or misuse.

The Public Health Security and Bioterrorism Preparedness and Response Act of 2002, was enacted to enhance controls over dangerous biological agents and toxins. Title II, subtitle B of the Act,⁶ addressed the lack of authority for the Secretary of Agriculture, under legislation effective at that time, to regulate possession of biological agents and toxins that pose a severe threat to plant or animal health. The Act requires the Secretary to both establish and enforce safeguard and security measures to prevent access to select agents. On December 13, 2002, APHIS published an interim final rule setting forth the regulations for possessing, using, and transferring select agents. The regulations addressed standards and procedures that registered entities must follow to safeguard and secure the select agents.

For our Phase I review, we reported that APHIS granted provisional registrations to entities without determining whether their security plans provided adequate safeguard and security measures. During our site visits in Phase II, we found that none of the 10 entities we reviewed had fully complied with the regulations. We selected 10 of 75 entities registered with APHIS, and performed site visits to test the entities' compliance with the regulations and to determine whether security controls were adequate and functioning. We found that security plans (1) were not based on site-specific risk assessments as required, (2) did not address critical areas required by the regulations, and (3) were not performance tested or reviewed and updated annually by the registered entities (see Finding 4).

⁶ Also known as "The Agricultural Bioterrorism Protection Act of 2002."

APHIS had not performed timely reviews of security plans to determine whether the plans were sufficient and had not timely followed up with the entities to address any deficiencies. This occurred because APHIS officials believed that the regulations intention to “minimize disruption of research” took precedence over the need to fully comply with the regulations. Therefore, APHIS only reviewed the initial registration applications to determine if a security plan was submitted. APHIS did not perform more thorough reviews until several months after the initial registrations, at that time identifying significant deficiencies in the plans. For example, one entity submitted an initial registration package on March 12, 2003. The entity submitted its Biosafety and Security Plan in a subsequent submission on May 27, 2003.⁷ On September 29, 2004, nearly 16 months after the registration was submitted, APHIS sent a letter to the entity with 56 action-items or items needing clarification and 8 recommendations. Thirty-three of the 56 action items and 4 of the 8 recommendations related to the Biosafety and Security Plan. The remaining items and recommendations were related to the initial registration package. The APHIS letter provided the entity 10 business days to respond. However, the entity was not able to provide their response until November 19, 2004. During our site visit in December 2004, we identified significant deficiencies in the security plans, such as the lack of procedures to report and remove suspicious persons, and the lack of procedures for reporting and investigating unintentional and/or inappropriate release of select agents.

Registered entities we visited expressed concerns regarding APHIS oversight, including inadequate guidance to implement the select agent rules, untimely review and response to required submissions, and insufficient timeframes for responding to APHIS inquiries. Inadequate guidance and untimely reviews of security plans may have contributed to some of the deficiencies we identified. However, we noted that, in many cases, deficiencies were due to the entities not following regulatory requirements. Even though each had been inspected by APHIS for compliance with the regulations prior to our review, we identified a number of security deficiencies at the sites visited. We found that registered entities:

1. did not adequately restrict access to select agents or toxins as required by the regulations (Finding 5);
2. did not maintain adequate inventories of select agents (Finding 6); and
3. did not maintain adequate documentation concerning Biocontainment or Biosafety and Security training (Finding 7).

For our Phase I review, we reported that APHIS had not established policies and procedures to ensure that inspections of the registering entities’ security

⁷ In 9 CFR §121.0(d), the RO was required to submit the security section of the Biosafety and Security Plan by June 12, 2003.

measures were consistent and thorough. Inspections performed by APHIS did not provide clear documentation concerning the nature or extent of deficiencies, and did not always conclude as to whether security measures implemented by the registered entities were adequate. We also reported that although some inspections revealed deficiencies, APHIS did not always notify the registered entities of the results of the inspections and address, in writing, the nature of the deficiencies or the requirements for followup.

Subsequent to our site visits, final regulations were issued on March 18, 2005. The final regulations provide additional guidance to entities to help ensure that the provisions of the Act and applicable regulations are fully implemented. For example, the final regulations provide clarification for issues such as inventory control requirements for select agents, and state that additional guidance will be forthcoming for issues such as security required for select agents or toxins. In addition, APHIS and CDC are working with interagency groups and security experts to draft a document that will provide additional guidance about the security required for select agents or toxins. Even though the guidance was to be available in spring 2005, it was not completed as of August 12, 2005.

In the Phase I report, we recommended that APHIS establish formal procedures for performing security inspections at the registered entities in order to ensure that the inspections are consistent and thorough, and that documented and supportable conclusions are made concerning the adequacy of security measures. We concluded that the issues identified during our site visits in Phase II confirm the need for thorough and consistent inspections as recommended in the Phase I report. Because of the noncompliance issues we identified in Findings 4 through 7, we are recommending that APHIS re-inspect the registered entities. Re-inspections of entities' security plans and procedures should be done using formal procedures established to ensure consistent and thorough reviews (as recommended in Phase I, Audit No. 33601-2-At). The inspections should also ensure that conclusions are drawn regarding whether security is adequate, and corrective action plans should be developed and followup performed to ensure deficiencies are corrected.

Recommendation 1

Re-inspect registered entities to ensure compliance with regulations regarding the security over select agents. The inspections should be done using formal written procedures to ensure consistent and thorough reviews. In our Phase I report we recommended that formal procedures be developed.

Agency Response. In its December 2, 2005, response, APHIS stated:

Per direction from the Office of Management and Budget, APHIS must coordinate entity inspection policy with * * * CDC. To date, CDC has not agreed to total re-inspection of all current registrants. Also, good regulatory policy and resource constraints dictate that we adopt a risk based re-inspection policy. APHIS will re-inspect a registered entity upon submission of either an amendment, which includes the use of an agent or activity of higher risk and/or work in a new area. Also, APHIS will re-inspect entities when evidence suggests there is a compliance issue or when an entity has requested amendments that results in a "higher risk" level of activity. This will be effective immediately. In the event that there are no compliance issues or registration amendments, we will re-inspect each no less than every * * * [2] to * * * [3] years consistent with the registration schedule. This combination of risk-based and regularly scheduled re-inspection plan would provide sufficient security and result in most entities being re-inspected within the next * * * [2] years. All re-inspections will be conducted under formal procedures.

OIG Position. We cannot accept management decision for this recommendation. The Secretary of Agriculture is required to establish and enforce security measures to prevent access to select agents. Our review at 10 registered entities identified several compliance issues that were not identified during inspections performed prior to our visits to the registered entities. APHIS inspections, if performed in a consistent and thorough manner, should provide primary evidence for determining if adequate security has been implemented at the registered entities. Without such inspections, the agency would not have the means to gather sufficient evidence that would "suggest there is a compliance issue" at a specific registered entity. Therefore, APHIS should re-inspect registered entities using formal written procedures to provide for consistent and thorough inspections and to gather sufficient evidence to conclude whether adequate security measures have been implemented. We agree that in performing the re-inspections, a risk-based strategy would be prudent so that entities possessing select agents with a higher level of risk would be re-inspected first. In order to reach management decision for this recommendation, please provide a plan for re-inspecting APHIS registered entities using formal procedures and the timeframes for completing the re-inspections.

Finding 2**APHIS Had Not Kept Up-to-date Data Pertaining to Individuals Who Have Access to Select Agents or Toxins**

APHIS had not updated its list of individuals authorized to access select agents or toxins. On October 8, 2004, APHIS provided us a current list of approved individuals granted access to select agents or toxins (authorized list). However, we found that the APHIS list did not always agree with the lists maintained by the registered entities. We found that APHIS had not updated the list for 5 of the 10 entities we reviewed. This occurred because (1) APHIS did not update the lists when notified by the entities that certain individuals no longer had access to the select agents or toxins or (2) the entities did not notify APHIS of individuals no longer having access. We found that APHIS had not developed written policies and procedures for accurately and promptly updating authorized lists subsequent to entity requests that individuals needing access be added to the list or that the access status for individuals no longer needing access be changed from active to inactive. As a result, APHIS does not have accurate information to use in monitoring registered entities' compliance with requirements for restricting access to the select agents.

The Act⁸ states that APHIS regulations shall include provisions to ensure that registered entities provide access to select agents or toxins to only those individuals whom the RO determines have a legitimate need to handle or use such agents and toxins. In accordance with requirements of the Act, APHIS' regulations⁹ state that, for each individual identified by the RO as having a legitimate need to handle or use select agents, the RO must submit the individual's name and identifying information to APHIS¹⁰ and the U.S. Attorney General. The U.S. Attorney General then determines whether the person is a "restricted person" as defined in the Act.¹¹ Once the determination is made, APHIS is notified, and in-turn, notifies the registered entity of whether access is granted or denied. The legislation and regulations further provide that the names of individuals having access to select agents be submitted to the U.S. Attorney General for review at least every 5 years. APHIS is responsible for notifying the RO if an individual is granted full or limited access, or denied access, to biological agents or toxins, and will notify the individual if he/she is denied access or granted only limited access to such agents or toxins.¹² APHIS regulations state that the RO must immediately notify the agency when access is terminated and the reasons for termination.¹³

⁸ Section 212(e)(2) and (3) of Public Law 107-188.

⁹ APHIS regulations 7 CFR 331.10(d) and 9 CFR 121.11(d)

¹⁰ For overlap agents, names can either be submitted to APHIS or CDC.

¹¹ Restricted persons are defined by the Act as individuals within certain categories as defined by various *United States Code* citations. These categories include people who have committed certain crimes, people who have known ties to domestic or international terrorist organizations, and persons determined to be an agent of a foreign power.

¹² APHIS regulations 7 CFR 331.10(g) and 9 CFR 121.11(g), issued December 13, 2002.

¹³ APHIS regulations 7 CFR 331.10(k) and 9 CFR 121.11(l).

APHIS maintains (on an electronic spreadsheet) the listing of individuals that have been approved or denied access to select agents or toxins. In confirming the accuracy of the spreadsheet with the list maintained by the 10 entities visited,¹⁴ we found that the agency's spreadsheet provided to us on October 8, 2004, was not up to date for 5 of the 10 entities.

- At one entity, we compared the list provided by APHIS (dated October 2004) to a listing provided by the registered entity dated June 2004. We found that seven individuals shown as active on APHIS' list were not included on the entity's list. The RO told us that periodic reports were sent to APHIS updating the entity's authorized list with individuals either being added or deleted from the list. For one of the individuals on the list, we were given a letter to APHIS dated June 3, 2004, telling the agency to remove the person from their active list. The entity neither had documentation showing that the other six inactive individuals had been reported to APHIS, nor had documentation giving the reasons access was terminated. We were told by entity officials that access was terminated for the individuals because they were no longer working with the agents because of transfers to other positions within the entity or they had taken jobs with other entities.
- At another entity, we found inaccuracies and out-of-date data when we compared the access list prepared and maintained by the entity and the list APHIS provided the entity subsequent to requested modifications. We found discrepancies in identification numbers, employee status (active/inactive), and names. For example, the institution submitted documentation to APHIS to remove an individual from the authorized list in August 2004. APHIS acknowledged the request during the same month. However, APHIS' November 2004 list, showed the individual as current with unrestricted access. Entity officials stated that errors appearing on the authorized list from APHIS were common. Based on our evaluation, we concluded that APHIS is not reviewing or maintaining adequate controls over the authorized list.

Although it is the responsibility of the RO to ensure only APHIS approved individuals are granted access to select agents or toxins, it is incumbent upon APHIS to promptly and accurately update the list based on requested changes from the registered entities. Registered entities seek to add individuals to the list or to show individuals inactive once access to the select agents is terminated. Since we identified instances where APHIS had not adequately updated the authorized lists subsequent to requested changes

¹⁴ Site visits were performed in November and December 2004.

(additions/deletions), we concluded that APHIS' controls over the authorized lists do not lend assurance that the list is adequately updated to reflect the most current information presented to APHIS by the registered entities. By not ensuring accurate and up-to-date lists of approved individuals, APHIS cannot assure the public that access is restricted to approved individuals and that select agents or toxins are secure and adequately safeguarded from theft and/or unauthorized use.

Recommendation 2

Develop and implement written policies and procedures to ensure authorized lists are accurately and promptly updated. The procedures should include requiring the entities to verify APHIS records, and either provide corrections or attest to the accuracy of the list.

Agency Response. In its December 2, 2005, response, APHIS stated:

APHIS agrees with this recommendation. The National Select Agent Registry (NSAR) will become functional by December 30, 2006. The NSAR will contain all of the information found on the registration application documents, which include all of the authorized individuals. The * * * RO and the alternate responsible official (ARO) will have access to this system in order to update and verify the accuracy of the data. APHIS will request programming modifications that will allow notices to be sent out quarterly to entities that require verification of their section 4B. This will be completed by December 30, 2006.

OIG Position. We accept management decision for this recommendation.

Finding 3

APHIS Had Not Properly Safeguarded Sensitive Data Regarding Individuals Authorized to Possess, Use, and Transfer Select Agents or Toxins

APHIS had not adequately safeguarded sensitive security and personal information pertaining to individuals authorized to possess, use, or transfer select agents or toxins. We identified two instances where information regarding authorized individuals was provided to the wrong registered entity. This occurred because of human error, which we attributed in part to the fact that APHIS had not developed a national database of registered entities containing critical information including the names of individuals authorized

to access select agents at the particular entity.¹⁵ Until the national database is developed, APHIS will have to continue to rely on a mix of manual records and computerized spreadsheets maintained separately while administering the select agent program. Also, APHIS had not established internal controls, in the form of policies and procedures, to prevent such occurrences. As a result, there is a greater risk that sensitive information is inadvertently disclosed in violation of the Act.

According to the Act, USDA (among other agencies) shall not disclose information that identifies the select agent or toxin possessed, used, or transferred by a specific person or “discloses the identity or location of a specific person.”¹⁶

We identified two instances where APHIS provided personal and security information to the wrong registered entities. This occurred because of human error. Currently information regarding security clearances for individuals is maintained on an electronic spreadsheet, separate from hardcopy files maintained for each registered entity. The data has not been incorporated into a single database of registered entities. In our Phase I report, we reported that APHIS had not developed a national database of registered entities, as required by the Act. The purpose of the database is to facilitate the identification of the agents and their location, as well as their source. In our Phase I report, we concluded that the absence of the database diminishes APHIS’ ability to effectively monitor compliance with safety and security requirements. During our Phase II review, we concluded that the absence of the database contributed toward APHIS erroneously providing sensitive information to the wrong entities. If the information had been maintained as part of a comprehensive and organized database, the likelihood of this type of error could have been reduced.

In Phase I, we also reported that, because APHIS had not designated a single RO for the select agent program, the agency had not issued instructions or procedures for implementing the Act. The absence of agency policies and procedures weakens APHIS’ ability to ensure applicable laws and regulations are followed. Internal control comprises plans, methods, procedures, and actions to meet objectives such as ensuring compliance with applicable laws and regulations.¹⁷ For Phase II, we concluded that the establishment of an adequate system of internal controls could have prevented the two violations of the Act we identified during our site visits.

- On November 15, 2004, APHIS mistakenly faxed a list of all of the people approved for access (the authorized list) at a non-profit research hospital along with their identification numbers, which are

¹⁵ This condition was identified in our Phase I report (Audit No. 33601-2-At).

¹⁶ Public Law 107-188, June 12, 2002, section 212, (h) (1) (A).

¹⁷ “Standards for Internal Control in the Federal Government,” published by the General Accountability Office in November 1999.

used by the FBI for background checks to one of the academic institutions in our sample. Two of the academic institution's employees that were to be added to the list of employees approved to work with select agents or toxins were included on the erroneously faxed list from the research hospital. The following day, APHIS faxed a new list with only the academic institution's approved individuals, including the two newly approved employees.

- Also on November 15, 2004, APHIS mistakenly faxed one page listing individuals for another institution. The list was a printout of APHIS' electronic spreadsheet, and included the individuals' names, identification numbers, other personal information, and the access and security status of the individuals (i.e., restricted or unrestricted access). The academic entity's officials told us that they informed APHIS officials of the mistake and were told to return the list.

Recommendation 3

Develop and implement internal controls designed to prevent the release of sensitive security information associated with registered entities.

Agency Response. In its December 2, 2005, response, APHIS stated:

APHIS agrees with this response. The NSAR will prevent accidental release of another entity's information. For those entities that are not using the NSAR to register or amend their application, a protocol will be developed that requires second party verification of any sensitive information that is sent to an entity. This protocol will be developed by March 30, 2006.

OIG Position. We accept management decision for this recommendation.

Section 2: Registered Entities' Compliance With Select Agents or Toxin Regulations

During this phase of our audit, we also made field visits to 10 registered entities where select agents or toxins are used or stored to examine registered entities' compliance with the regulations. The purpose of the visits was to determine whether APHIS had adequate controls to ensure compliance with the regulations. We identified compliance issues including:

1. Biosafety/Biocontainment and Security Plans did not comply with regulatory requirements;
2. Registered entities did not adequately restrict access to select agents or toxins as required by the regulations;
3. Registered entities did not maintain adequate documentation concerning Biocontainment/Biosafety and Security training; and
4. Registered entities did not maintain adequate inventories of select agents.

Even though APHIS inspected 9 of the 10 registered entities and CDC had inspected the other entity prior to our field visits, the conditions we noted were seldom identified by the inspections. For Phase I of our review, we reported that APHIS had not established policies and procedures to ensure that inspections of the registering entities' security measures were consistent and thorough, and that APHIS inspections were not sufficiently documented to show whether registered entities had implemented adequate safeguard and security measures. We also reported that inspections performed by APHIS did not provide clear documentation concerning the nature or extent of deficiencies, and did not always conclude as to whether security measures implemented by the registered entities were adequate.

We concluded that more thorough inspections would help APHIS better identify and address compliance issues at the registered entities. Therefore, several of our recommendations in Finding Nos. 4 through 7 address ways of improving the inspection process. Because the Act requires APHIS and CDC to develop and implement procedures to share responsibilities for inspecting entities that handle overlap agents, we met with officials from the HHS-Office of Inspector General (OIG) to coordinate our recommendations. HHS-OIG conducted reviews of entities registered with CDC and identified issues with inspections similar to those identified during our reviews of entities registered with APHIS.

Finding 4**Biosafety/Biocontainment and Security Plans Did Not Comply With Regulatory Requirements**

During our site visits, we noted a number of deficiencies regarding the entities' security plans. We found that security plans (1) were not based on site-specific risk assessments as required, (2) did not address critical requirements required by the regulations, and (3) were not performance tested or reviewed and updated annually. Registered entities in our sample gave various reasons for deficiencies in their plans, including the lack of sufficient guidance from APHIS. Based on the results of our site visits and the deficiencies we found in the security plans, we concluded that APHIS had not provided the entities with timely feedback on the sufficiency of the plans, and had not provided sufficient guidance for completing the plans in accordance with the regulations. Because of the deficiencies in the plans, there is reduced assurance that security measures at registered entities are adequate to mitigate risks of unauthorized access to the agents or toxins.

The Act requires that USDA establish and enforce safety procedures for select agents or toxins, including appropriate skills to handle agents and toxins, and proper laboratory facilities to contain and dispose of agents and toxins. In addition, the Act requires that USDA establish and enforce safeguard and security measures to prevent access to select agents or toxins for use in domestic or international terrorism or for any other criminal purpose. Pursuant to section 212(e)(1) of the Act, the safeguard and security requirements must be commensurate with the risk posed by the agent or toxin. As a condition of registration, the RO must develop and implement a Biocontainment/Biosafety¹⁸ and Security Plan. The plans must contain sufficient information and documentation to describe the biosafety and containment procedures, and the security systems and procedures.

As we reported in our Phase I report (Audit No. 33601-2-At), APHIS granted provisional registrations to entities without determining whether their security plans provided adequate safeguard and security measures. Regulations allowed for provisional registration if an entity could show by November 12, 2003, that the entity had provided the Attorney General with all of the documentation required to conduct security risk assessments and had otherwise met all of the requirements of the regulations. However, APHIS officials stated that the regulation's intention to "minimize disruption of research" took precedence over the need to fully comply with security requirements by the deadline. Consequently, APHIS reviewed registration applications only to ensure a security plan had been submitted, not that it met the requirements of the regulations. As a result, the agency had not taken

¹⁸ APHIS regulation 7 CFR 331.11 requires a biocontainment plan for plant pathogens. APHIS regulation 9 CFR 121.12 requires a biosafety plan for animal and overlap agents and toxins.

sufficient action to ensure that registered entities have implemented adequate safeguard and security measures to comply with the legislation and regulations.

In promulgating the interim final rule, APHIS concluded that because different agents and toxins pose differing degrees of risk, depending on factors such as their escape potential and availability of a suitable habitat (for plant-related agents) and transmission and effect of exposure to the agent or toxin (for overlap and animal agents or toxins), it would be counterproductive to attempt to prepare a detailed list of prescriptive requirements for entities (i.e., a “one size fits all” design standard). Instead, APHIS established a set of performance standards to be addressed while considering the degree to which they were appropriate to the risks presented by a particular agent or toxin, given its intended use and the location of the entity. Therefore, risk assessments were crucial to the development of security plans sufficient to mitigate vulnerabilities and fully address the established performance standards. We found that 7 of the 10 entities did not base their security plans on site-specific risk assessments.

To address the performance standards and comply with the regulations, entities’ Biocontainment/Biosafety and Security Plans must describe critical requirements such as, inventory control procedures, personnel suitability for those individuals with access to select agents or toxins, physical security, as well as other areas. We found that 7 of the 10 entities lacked documented policies and procedures for critical requirements identified in the regulations.

Finally, to ensure that the plans continue to meet the entities’ containment and security needs, APHIS requires that the plans be reviewed, performance tested, and updated annually. The plans must also be reviewed and revised, as necessary, after any incident. We found that 4 of the 10 entities either did not performance test the security plans or did not annually review and update their plans.

The final rule, issued on March 18, 2005, stated that APHIS and CDC were working with interagency groups and security experts to draft a document to provide additional guidance about the security required for select agents or toxins. Even though the guidance was to be available in spring 2005, it was not completed as of August 12, 2005. The 5th edition of the “Biosafety in Microbiological and Biomedical Laboratories”, which is under development, will provide additional guidance on laboratory security.

Security Plans Were Not Based on Site-Specific Risk Assessments

We found that 7 of the 10 entities we reviewed did not base their security plans on site-specific risk assessments. APHIS regulations¹⁹ require that entities' security systems and procedures must be designed according to a site-specific risk assessment and must provide graded protection in accordance with the threat posed by the agent or toxin. The regulations state that a site-specific risk assessment should involve a threat assessment and risk analysis in which threats are defined, vulnerabilities examined, and risks associated with those vulnerabilities are identified. The interim final rule required that security systems and procedures must be tailored to address site-specific characteristics and requirements, ongoing programs, and operational needs and must mitigate the risks identified by the assessments. The following are examples of the deficiencies we found.

- One registered entity based its security systems and procedures on security measures in place prior to September 11, 2001. The entity's officials claimed that lack of guidance from APHIS regarding specific requirements for site-specific risk assessments and the costs of having a risk assessment performed by an outside consultant were barriers to completing a formalized risk assessment. APHIS' inspection checklist prepared October 2003 showed that the entity's security plan was based on a site-specific risk assessment.
- At another entity for which a site-specific risk assessment was not prepared, we found that the security plan described physical security measures that included guarded entrance gates and perimeter fencing. However, the facility did not have these security measures. The plan actually describes security features at another of the entity's facilities. The entity had used the plan from another facility, had not performed a site-specific risk assessment for that location, and had not addressed the vulnerabilities at that particular site. APHIS has prepared two inspection checklists, including one in October 2003 and one in December 2003. The October 2003 checklist indicated that the security plan was based on a site-specific risk assessment, and the December 2003 checklist indicated that the risk assessment was not site specific.
- The RO at one entity said that the entity had not had the resources to perform a site-specific risk assessment. He said that the entity was just starting an assessment at the time of our audit. During our visit to this entity, we found that vials of Exotic Newcastle Disease were stored in a freezer in an area with unrestricted access. The location of the freezer was not identified in the entity's security plans, and there

¹⁹ Title 7 CFR 331.11(a)(2) and 9 CFR 121.12(a)(2), issued December 13, 2002.

was no determination of the risk associated with storing the select agent in an area that was accessible to unauthorized individuals. APHIS' inspection checklist prepared in October 2003 showed that the entity's security plan was based on a site-specific risk assessment.

APHIS' interim rule dated December 13, 2002, stated that risk assessments should include a threat assessment and risk analysis in which threats are defined, vulnerabilities examined, and risks associated with those vulnerabilities are identified. It also stated that the security systems and procedures must be tailored to address site-specific characteristics and requirements and must mitigate risks identified by the risk assessments. However, APHIS' final rule issued on March 18, 2005, deleted these requirements and substituted the requirement that the security plan be designed according to a site-specific risk assessment and provide graded protection in accordance with the risk of the select agent or toxin, given its intended use.

Even though we agree that the site-specific risk assessments should provide protection in accordance with the risk of the select agent or toxin, we believe that the risk assessments should not only take into account the "intended use" of the biological agent, but should address vulnerabilities associated with the potential unintended use, such as the consequences of terrorists acquiring a particular agent and using it as a weapon. This would be in line with the intent of the Act. The Act gave the Secretary of Agriculture authority to regulate the possession of biological agents that, through acts of bioterrorism, could have a devastating impact on the domestic agricultural economy.²⁰ In addition, the Act specifically requires the establishment and enforcement of safeguard and security measures to prevent access to such agents and toxins for use in domestic or international terrorism or for any other criminal purpose. Therefore, APHIS should ensure that entities conduct risk assessments that adequately address vulnerabilities and mitigate risks of unauthorized individuals accessing and acquiring select agents for use in terrorism.

Security Plans Did Not Address Critical Requirements in the Regulations

During field visits we found that security plans for 7 of the 10 registered entities' lacked documented policies and procedures for critical requirements identified in the regulations. To address the performance standards and comply with the regulations, the Biocontainment/Biosafety and Security Plans must describe inventory control procedures, personnel suitability for those individuals with access to select agents or toxins, physical security, and cyber security. The plan must also contain provisions for securing the area (e.g., card access, key pads, locks) and protocols for changing access

²⁰ House of Representatives Conference Report No. 107-481, dated May 21, 2002.

numbers or locks following staff changes; procedures for loss or compromise of keys, passwords, combinations, etc.; procedures for reporting suspicious persons or activities, loss or theft of select agents or toxins, release of select agents or toxins, or alteration of inventory records; provisions for the control of access to containers where select agents or toxins are stored; provisions for routine cleaning, maintenance, and repairs; and procedures for reporting and removing unauthorized persons. We observed the following.

- One entity claimed that a staff vacancy resulted in elements of the security plan not being developed. The RO stated that the biosafety officer who was responsible for conducting the risk assessment had resigned and the position had remained vacant for over a year. The entity's plan lacked procedures for reporting incidents, such as releases of select agents, and security breaches. The plan also did not contain security training procedures. A September 23, 2004, letter from APHIS also recommended that the entity develop a sign-in/out log for after-hour and weekend activity employees; expand card-key access controls to all select agent areas; develop restricted access policy and procedures support units, such as maintenance and custodial staff; and to complete comprehensive incident response plans for the select agents. In contrast to the September 2004 letter, an APHIS inspection checklist prepared in October 2003 showed that the entity's security plan contained all the critical elements required.
- At another entity, we found that critical requirements were missing from the security plans, including procedures for (1) notifying APHIS and CDC when individuals' access was terminated, (2) changing access numbers or locks when staff left, (3) addressing the loss or compromise of keys or combinations, (4) reporting suspicious activities, and (5) removing unauthorized individuals from select agent or toxin areas. APHIS' inspection checklist prepared in October 2003 showed that the entity's security plan contained all the critical elements required.

Security Plans Were Not Performance Tested or Reviewed and Updated as Required

We found that 4 of the 10 entities either did not performance test the security plans or did not annually review and update their plans. Regulations require that Biocontainment/Biosafety and Security Plans must be reviewed, performance tested, and updated annually. The plan must also be reviewed and revised, as necessary, after any incident. The following examples are some of the conditions noted for entities that did not performance test or did not annually review and update plans.

- One entity had not updated the security plan annually as required by regulation. The last update of the plan was the version submitted on June 2003. APHIS' security checklist prepared in October 2003 showed that the security plan had not been tested or updated. However, the RO stated that the plan had not been updated because they thought it was adequate since they had not received any feedback from APHIS. However, during the time of our site visit, the entity received a letter from APHIS, dated November 15, 2004, noting a number of deficiencies in the plan and recommending sign-in/out procedures and protocols be developed for after-hours activities, electronic monitoring and access controls be installed in select agent activity areas, locks be installed in specified laboratory rooms, and the number of individuals having access to the select agent activity areas be verified (noting that a substantial number of people appear to have access to some areas).
- At another institution, the assistant RO stated that they periodically checked entryways and prohibited areas to ensure that doors were locked. However, there were no procedures to review and evaluate other procedures in the security plan. APHIS' security checklist prepared in October 2003 did not include any deficiencies regarding testing and updating security plans.

The final regulations published on March 18, 2005, require that drills or exercises must be conducted at least annually to test and evaluate the effectiveness of the plan. The plan must be reviewed and revised, as necessary, after any drill or exercise and after an incident. APHIS will need to ensure that these new requirements are included in the registered entities' procedures and determine that the procedures have been implemented when APHIS inspections are performed.

Recommendation 4

Provide registered entities specific guidance for performing risk assessments, including instructions for performing site-specific risk analyses. APHIS' guidance should provide advice on how to perform threat assessments and identify vulnerabilities, and suggest security measures that could help to mitigate risks.

Agency Response. In its December 2, 2005, response, APHIS stated:

APHIS agrees with this recommendation. CDC has requested that APHIS participate in a meeting on March 6 - 8, 2006, in order to provide better guidance to entities in the following areas: agent specific risk/threat assessment; IT and records security; risk mitigation and screening of individuals; and

compliance issues and tools. The meeting, as currently planned, will include security specialists from the federal and state governments. Using the materials generated from this meeting, APHIS (and CDC) will provide guidance to entities on risk assessment by December 1, 2006. Finalization is dependent on receiving concurrence from CDC.

OIG Position. We cannot accept management decision for this recommendation. Although the planned meeting with CDC should be helpful in establishing guidance to entities for establishing security procedures, the response addressed “agent specific risk/threat assessments” rather than site-specific risk assessments. We found that 7 of 10 entities we visited did not perform site-specific risk assessments to address the physical characteristics of the areas where the select agents were used or stored. In order to reach management decision, please indicate whether the guidance will include instructions on performing risk assessments based on the physical characteristics of each site (e.g., laboratories and storage areas) housing select agents. Also, we cannot accept management decision for corrective action that is contingent upon receiving concurrence from CDC. In this circumstance, the recommendation must remain open until a detailed time-phased corrective action plan has been developed.

Recommendation 5

In developing policies and procedures for reviewing and inspecting entities’ compliance with the regulations, APHIS should include steps to ensure registered entities base their security plans on a site-specific risk analysis. Site specific risk analyses should be examined to ensure that entities perform threat assessments that address its vulnerabilities. APHIS should also ensure that security plans are developed that will mitigate the risks identified and help to prevent unauthorized individuals from accessing and acquiring select agents or toxins for use in terrorism. APHIS’ inspection reports should conclude whether entities’ security plans were based on the results of site-specific risk analyses performed in accordance with the guidance issued.

Agency Response. In its December 2, 2005, response, APHIS stated:

APHIS agrees with this recommendation. In response to Recommendation 4, APHIS is working with CDC to provide guidance to entities regarding the risk assessment process. Based on these guidance documents, improved guidance for inspectors will be documented in the CDC/APHIS Operational Plan. This will be completed by December 1, 2006. Finalization is dependent upon receiving concurrence from CDC.

OIG Position. We cannot accept management decision for this recommendation. Although the response states that APHIS agrees with the recommendation, it does not specifically address whether APHIS will include steps in the inspections to (1) ensure that registered entities base security plans on site-specific risk analysis, (2) ensure that registered entities perform threat assessments that address vulnerabilities, (3) ensure that security plans developed by registered entities provide measures to mitigate risks identified in risk assessments, and (4) conclude whether registered entities' security plans were based on the results of site-specific risk analysis performed in accordance with the guidance issued. Also, we cannot accept management decision for corrective action that is contingent upon receiving concurrence from CDC. In this circumstance, the recommendation must remain open until a detailed time-phased corrective action plan has been developed.

Recommendation 6

In developing policies and procedures for reviewing and inspecting entities' compliance with the regulations, APHIS should include steps to verify that the entities' security plans have thoroughly addressed all critical areas identified by the regulations. APHIS' inspection reports should conclude whether each critical area was adequately addressed.

Agency Response. In its December 2, 2005, response, APHIS stated:

APHIS agrees with this recommendation. A check list will be developed by June 30, 2006, that the APHIS Security Specialist will use when each entity is reviewed.

OIG Position. We cannot accept management decision for this recommendation. Although the response states that APHIS agrees with the recommendation, it does not specifically address whether APHIS will include steps in the inspections to verify that entities' security plans have thoroughly addressed all critical areas identified by the regulations. In addition, security plans should be reviewed during APHIS inspections to ensure that the plans being used by the entity contain all critical areas required by regulations.

Recommendation 7

In developing policies and procedures for reviewing and inspecting entities' compliance with the regulations, APHIS should include steps to verify that that entities are conducting and documenting annual performance tests of their security plans, and are updating plans based on the results of the performance tests, drills, or exercises. APHIS' inspection reports should conclude whether annual performance tests were performed and whether their results were appropriately utilized in updating security plans.

Agency Response. In its December 2, 2005, response, APHIS stated:

APHIS agrees with this recommendation. To provide better guidance to inspectors, APHIS and CDC will document operational procedures for review of annual drills and exercises conducted by an entity. These procedures will be finalized by September 30, 2006. Finalization is dependent upon receiving concurrence from CDC.

OIG Position. We cannot accept management decision for this recommendation. Although the response states that APHIS agrees with the recommendation, it does not specifically address whether APHIS will include steps in the inspections to verify that entities are conducting and documenting annual performance tests of their security plans and updating the plans based on the results of the tests. Also, we cannot accept management decision for corrective action that is contingent upon receiving concurrence from CDC. In this circumstance, the recommendation must remain open until a detailed time-phased corrective action plan has been developed.

Finding 5

Registered Entities Did Not Adequately Restrict Access to Select Agents or Toxins As Required by the Regulations

During our site visits, we found that 6 of the 10 entities' did not adequately restrict access to select agents. This occurred because three entities did not provide APHIS the names of all individuals so they could be cleared by Department of Justice for access to the select agents, and three entities did not implement adequate controls for restricting access to areas where select agents were stored or used. At one of the three entities that did not provide APHIS the names of all persons having access to the select agents, an unauthorized individual was allowed to perform experiments with the select agent. By not adequately restricting access to select agents, these entities increased the risk that select agents could be acquired and used in domestic or international terrorism.

The Act requires that the regulations include provisions to ensure that the registered entities provide access to select agents or toxins to only those individuals that have a legitimate need to handle or use such agents or toxins. APHIS regulations 7 CFR 331.10(a) and 9 CFR 121.11(a) provide that an individual may not have access to select biological agents or toxins unless approved by APHIS or, for overlap agents, APHIS or CDC. Regulations require the RO to ensure that only approved individuals within the entity have access to select agents or toxins. In addition, the RO must request such access for only those individuals who have a legitimate need to handle or use

select agents or toxins, and who have the appropriate training and skills to handle such agents or toxins.

The following are examples where registered entities were not adequately restricting access to select agents.

- At one entity, two unauthorized individuals were granted access to a laboratory with select agents, and one of the two individuals was given direct access to the select agent, without approval from the RO, and without clearance by the Attorney General. The RO was not aware that unauthorized individuals were given access to the laboratory. The principal investigator²¹ was aware of the situation and approved their access without clearance from the RO. One individual was allowed to conduct experiments using *Brucella abortus*.²² APHIS' inspection checklist prepared in August 2004 did not cite any deficiencies regarding access to the select agents.
- At another entity, we found that two individuals having access to sensitive information (i.e., locations of select agents, individuals granted access to the agents, security procedures) had not been reviewed by the Attorney General. APHIS' interim final rule issued December 13, 2002, did not require the RO to submit the names of individuals having access to sensitive information for clearance by APHIS and the Attorney General. During our site visit in November 2004, we discussed our concerns with the entity that the individuals had access to information that could allow them to gain access to the select agents. The entity agreed, and submitted the names to APHIS. The final regulations published on March 18, 2005, added that an individual is deemed to have access if he/she has the ability to gain possession of a select agent or toxin. We also found that four of the entity's employees still had access to the laboratory where select agents are used even though they no longer had a legitimate need to access that area. This occurred because the entity did not have controls in place to properly monitor electronic card authorization, removal, and verification (periodic review of the access log). As a result, the university has reduced assurance that dangerous biological agents and toxins, retained for research or held in culture repositories, are secure from unauthorized use or loss.
- During our visit to one facility, we found that 62 vials and 15 tissue cultures of Exotic Newcastle Disease²³ were stored in a long-term storage freezer in the basement. The freezer was locked with a

²¹ The principal investigator is the researcher in charge of the particular research project.

²² *Brucella abortus* is a contagious disease affecting cattle and bison. It is an overlap agent that also affects humans.

²³ According to an APHIS fact sheet dated January 2003, Exotic Newcastle Disease is probably one of the most infectious diseases in poultry. It is a fatal viral disease affecting all species of birds.

common padlock. The select agent was stored in an area that had not been identified on the entity's security plans, and was not in a secure area. The basement storage room was not locked during the day, and was accessible by many individuals who had not been approved to access select agents. The researcher stated that the vials had been moved to the storage area because they were not needed and were to be destroyed. The freezer had not been accessed in 2 to 3 months prior to our visit. Because of our inquiries concerning security over the select agent, the RO took action to destroy all but 15 vials of the agent, which were to be transferred to another registered entity. APHIS' inspection checklist prepared in August 2004 did not cite any deficiencies regarding access to the select agents. There was nothing in the inspection documentation to indicate whether this freezer had been identified and examined during the August 2004 visit by APHIS.

- Although one registered entity maintained a visitor's logbook of access to areas housing select agents, many of the logs were missing critical data, such as the date of the visit, time of the visit, or the signature of the visitor's escort. No one, such as a security guard, was monitoring the entries in the access logbook. Therefore, visitors accompanying authorized individuals may be gaining access into labs containing select agents or toxins without the knowledge of institution officials. We reviewed 476 recorded visits in the logbook and found that 27 were missing the date, 16 were missing time in and/or the time out, and 38 were missing an escort signature. Institution officials agreed that the visitor logs should be complete and up to date, but they stated that they were not overly concerned because an authorized individual must escort any visitor and only authorized individuals would have a key to enter the restricted areas. However, without a complete and accurate logbook, there is no accountability that only authorized individuals accompanied all visitors to the lab. During multiple APHIS inspections in October 2003, APHIS cited several deficiencies relating to restricting access such as the lack of security guards or employees present to control access into the facility. However, the inspection checklist showed that the entity had adequate controls regarding visitors. There was no indication that APHIS examined entries in the visitor's logbook during the inspection.
- At one entity, we were informed that the access logbook for periods prior to January 2004 was missing. The entity had reported to APHIS possession of the select agents (*Mycoplasma capricolum* and *Mycoplasma mycoides*)²⁴ in July 2002. The two researchers with access to the agent had transferred to another entity that was not registered to possess select agents. The laboratory manager had also

²⁴ *Mycoplasma capricolum* causes contagious caprine pleuropneumonia in goats and *Mycoplasma mycoides* causes contagious bovine pleuropneumonia in cattle, both highly infectious diseases.

transferred to another position at the same entity and no longer had access to the select agent. Prior to their transfer, one of the two researchers reported to the RO an unexplained discrepancy in the inventory records. The records were adjusted to reduce the select agent inventory by two vials. In a report to the RO, one of the former researchers wrote that the discrepancy was unexplained, but concluded that it was probably a clerical error since other such discrepancies had occurred. The report also concluded that there was limited access to the select agents and it was “extremely unlikely that someone could locate or procure these select agents surreptitiously.” The researcher’s report stated that they did not consider the discrepancy “to be of any concern regarding a breach of security.” The missing access logbook covered the period during which the discrepancy was noted, as well as another 10 months after the report was submitted to the RO. APHIS relied on an inspection performed by CDC in March 2003 even though the report did not make clear which laboratories were inspected and what was contained in those laboratories. There was no evidence that this storage area had been examined and no similar issues identified by CDC.

Recommendation 8

In developing policies and procedures for reviewing and inspecting entities’ compliance with the regulations, APHIS should include steps to compare its list of authorized individuals with the names of individuals having access to areas with select agents. This would include an examination of log books or other documented entries, as well as questioning researchers concerning which individuals can access the area. Inspectors should also examine the completeness and accuracy of access log books. Inspection reports should state whether security measures are adequate to restrict access to select agents only to authorized individuals.

Agency Response. In its December 2, 2005, response, APHIS stated:

APHIS agrees with this recommendation. To provide better guidance to inspectors, APHIS and CDC will document operational procedures that improve methods for verification of access controls used by the entity. These procedures will be finalized by September 30, 2006. Finalization is dependent upon receiving concurrence from CDC.

OIG Position. We cannot accept management decision for this recommendation. Although the response states that APHIS agrees with the recommendation, it does not specifically address whether APHIS will include steps in the inspections to compare its list of authorized individuals with the names of individuals having access to areas with select agents by examining

log books or interviewing researchers concerning access to the areas. The response also does not address whether APHIS' inspections would include an examination of log books or other documented entries to examine the completeness and accuracy of access records. In addition, we cannot accept management decision for corrective action that is contingent upon receiving concurrence from CDC. In this circumstance, the recommendation must remain open until a detailed time-phased corrective action plan has been developed.

Recommendation 9

In developing policies and procedures for reviewing and inspecting entities' compliance with the regulations, APHIS should include steps to identify and examine all areas where select agents are used or stored to ensure that access to those areas are properly secured. Inspection reports should specifically identify all areas containing select agents, state whether the areas are identified in the security plan and included in the site-specific risk assessments, and conclude as to whether security for each area is adequate.

Agency Response. In its December 2, 2005, response, APHIS stated:

APHIS agrees with this recommendation. To provide better guidance to inspectors, APHIS and CDC will document operational procedures for this phase of the inspection in the CDC/APHIS Operational Plan. These procedures will be finalized by September 30, 2006. Finalization is dependent upon receiving concurrence from CDC.

OIG Position. We cannot accept management decision for this recommendation. Although the response states that APHIS agrees with the recommendation, it does not specifically address whether APHIS will include steps in the inspections to identify and examine all areas where select agents are used or stored to ensure that the areas are properly secured. The response also does not address whether the inspection reports will identify all areas having select agents, state whether the areas are identified in the security plan and included in the site-specific risk assessment, and conclude as to whether security is adequate for each area. In addition, we cannot accept management decision for corrective action that is contingent upon receiving concurrence from CDC. In this circumstance, the recommendation must remain open until a detailed time-phased corrective action plan has been developed.

Recommendation 10

APHIS should conduct an investigation into the missing access logbook at the affected entity and, based on the outcome, make a determination as to the appropriateness of the entity's registration status.

Agency Response. In its December 2, 2005, response, APHIS stated:

APHIS agrees with this recommendation and will request that APHIS' Investigative and Enforcement Services staff conduct an investigation of this finding and submit its findings to the Associate Administrator by March 1, 2006.

OIG Position. We accept management decision for this recommendation.

Finding 6

Registered Entities Did Not Maintain Adequate Inventories of Select Agents

We found that 3 of the 10 registered entities in our sample did not adequately account for their inventories of select agents or toxins. This occurred because entity officials at one registered entity had not required researchers to keep track of select agent or toxin usage, and because of inaccurate inventory recordkeeping. Even though the entities were inspected by APHIS or CDC prior to our site visits, the inspection checklists did not identify the inventory deficiencies. As a result, without adequate accountability of select agent or toxin inventories, select agents may be lost or used for unauthorized purposes.

APHIS regulations²⁵ provided that the RO must maintain complete records of information necessary to give an accounting of all of the activities related to select agents. Such records must include accurate and current inventory records (including source and characterization data). We noted the following.

- One registered entity did not have inventory controls in place to track select agents. The current researcher maintained short hand records of the agents or toxins on hand and in use. This occurred because the researchers have not been required to maintain these records in the past and the entity had not developed and implemented an inventory system in compliance with current regulations. A detailed inventory system did not exist in recent years. As a result, there is no way to confirm exact amounts of each agent on hand at any given time to determine if there has been an incident of theft or loss. Additionally, the entity cannot readily provide an accounting of all current and past activities involving the agents they have been handling and storing. APHIS' inspection checklist prepared in October 2003 showed that the entity had a systematic approach to maintain a current, comprehensive system to track select agents.

²⁵ Title 7 CFR 331.14 and 9 CFR 121.15, issued December 13, 2002.

- At one entity, we found a repository containing 152 vials of biological material of which 31 vials were identified as select agents (26 vials were *Mycoplasma capricolum* and 5 were *Mycoplasma mycoides*); 20 vials as a non-select agent; and 101 vials for which the RO could not determine whether the biological material was or was not a select agent. We questioned the RO about the vials and she stated that they were part of a large repository that the registered entity had intended to ship to another entity. However, the other entity was not registered and the vials remained in storage. The RO stated that they were not sure what the other vials are so they are treating them as if they were select agents even though some of them may not be. Currently, these vials are stored in a freezer. We were told that the inventory had not been used since it was acquired. APHIS relied on an inspection performed by CDC in March 2003 even though the report did not make clear which laboratories were inspected and what was contained in those laboratories. There were no inventory deficiencies reported for this storage area.
- At another entity, we selected a sample of 10 entries in the inventory log. We traced the entries to the associated vials of select agent in the storage freezer. The researcher could not locate two vials. We were later told by the RO that the two missing vials were incorrectly recorded in the inventory since one was not a select agent and the other was incorrectly identified because inventory log numbers were transposed when the entry was made in the log. The RO acknowledged that the accounting for select agents needed to be improved. In response to the finding, the entity drafted a procedure to better account for select agents, which was awaiting approval and implementation. APHIS' inspection checklist prepared in October 2003 did not indicate any deficiencies regarding inventories.

APHIS amended the regulations to require the maintenance of an accurate, current inventory for each toxin held and for each select agent held in long-term storage (placement in a system designed to ensure viability for future use, such as in a freezer or lyophilized materials). The final regulations also provide more information about the types of information that must be included in the inventory records for each select agent or toxin. Under the new regulations, an inventory for a select agent must include the name and characteristics of the agent, the quantity acquired from another entity, where stored, when moved from storage and by whom, purpose of use, transfer records, etc., while an inventory for a toxin must include the name and characteristics of the toxin, the quantity acquired from another entity, the initial and current quantity, where stored, when moved from storage and by whom, transfer records, etc.

Recommendation 11

In developing policies and procedures for reviewing and inspecting entities' compliance with the regulations, APHIS should include steps to verify that the entities have established and implemented inventory controls and perform procedures to ensure that inventory records are accurate and up to date.

Agency Response. In its December 2, 2005, response, APHIS stated:

APHIS agrees with this recommendation. To provide better guidance to inspectors, APHIS and CDC will document operational procedures for this phase of the inspection in the CDC/APHIS Operational Plan. These procedures will be finalized by September 30, 2006. Finalization is dependent upon receiving concurrence from CDC.

OIG Position. We cannot accept management decision for this recommendation. Although the response states that APHIS agrees with the recommendation, it does not specifically address whether APHIS will include steps in the inspections to verify that the entities have established and implemented inventory controls and whether inspectors whether inspectors will perform procedures to ensure that inventory records are accurate and up to date. Also, we cannot accept management decision for corrective action that is contingent upon receiving concurrence from CDC. In this circumstance, the recommendation must remain open until a detailed time-phased corrective action plan has been developed.

Recommendation 12

For the entity with 152 vials of biological material (31 select agents, 20 non-select agents, and 101 unidentified agents), APHIS should conduct an investigation into the discrepancies, and work with the entity to determine whether the vials should be destroyed or transferred to another registered entity.

Agency Response. In its December 2, 2005, response, APHIS stated:

APHIS agrees with this recommendation and has investigated this finding. The entity was storing unknown agents as "select agents." The select agent regulations do not prevent this. Thus, no violation of the regulations have occurred.

OIG Position. We cannot accept management decision for this recommendation. Although the response states that APHIS agrees with the recommendation and has investigated this issue, it does not specifically state whether APHIS and the registered entity have worked together to determine

the disposition of the vials. In order to reach management decision for this recommendation, please provide information on what steps have been taken or are being taken to destroy or transfer the vials of select agents.

Finding 7**Registered Entities Did Not Maintain Adequate Documentation Concerning Biocontainment/Biosafety and Security Training**

We found that 6 of the 10 entities had not documented Biocontainment/Biosafety and Security training as required, and 2 of the 6 entities did not provide the required training for all individuals having access to the select agents or toxins. APHIS regulations require that entities provide safety/containment and security training²⁶ and that records of the training be complete and up to date.²⁷ We found that the ROs were not fully aware of the requirements related to annual staff training specified in the regulations and did not recognize the need to document the limited training that was provided. APHIS had not provided guidance on what constitutes appropriate training and the need for accurate training records. As a result, although staff may have the educational and work experience backgrounds needed to perform the basic technical requirements of operating a biological laboratory, there is no assurance that they have received training on current technological changes or procedural requirements concerning biocontainment, biosafety and security procedures regarding select agents or toxins. Without such training, not only is the safety and security of individuals working with the select agents or toxins at risk, but also the select agents or toxins may be vulnerable to misuse or mishandling.

According to the regulations²⁸, the RO must provide appropriate training in containment and security procedures to all individuals with access to select agents or toxins. Training must be provided to an individual at the time the individual is assigned to work with a select agent or toxin, and refresher training provided annually. The RO must maintain complete, up-to-date records of information necessary to give an accounting of all of the activities related to select agents or toxins listed, including training records for the individuals having access to the pathogens.²⁹

The following are examples of our observations regarding security training.

- At one entity, there was insufficient documentation to show that individuals were provided the proper training. Because of the large number of individuals having access to the select agents or toxins, we

²⁶ APHIS regulations 7 CFR §331.12 and 9 CFR §121.13, issued December 13, 2002.

²⁷ APHIS regulations 7 CFR §331.14(a)(3) and 9 CFR §121.15(a)(3), issued December 13, 2002.

²⁸ APHIS regulations 7 CFR 331.12 and 9 CFR 121.13.

²⁹ APHIS regulations 7 CFR 331.14 and 9 CFR 121.15.

were not able to confirm during our site visit, that everyone had the required training. In response to our inquiries, the RO developed a checklist to be used to track future training. At the time of our visit, the checklist had not been incorporated into the entity's standard operating procedures. APHIS performed multiple inspections at this registered entity in October 2003, and from October to December 2004. Checklists prepared during these inspections all showed that training was properly documented.

- At another entity, the initial training was not documented, and the entity was not providing annual refresher training as required. The entity's biosafety officer stated that the researchers were required to read the laboratory safety plan when they were initially assigned to work with any biological agents or toxins. There was no specific training for containment or security procedures aside from the requirement that individuals with access to select agents or toxins read policies and directives in the security plan. There was no process to confirm that the individuals had read the required procedures or had otherwise been informed about its provisions relating to containment and security procedures. APHIS' inspection checklist prepared in August 2004 showed that annual security awareness training was provided to all employees and that the training was properly documented.

We noted that regulations do not define what "appropriate training" would represent, and according to one entity's RO, APHIS has not provided any specific guidance on what would meet the requirement of "appropriate training". APHIS had not issued any guidance regarding training, other than the regulations. We concluded that training and documentation of training is not being provided consistent treatment at the registered entities we visited. It is the responsibility of the RO at each registered entity to ensure that individuals who handle or use select agents or toxins have the appropriate training and skills.

Final regulations published on March 18, 2005, state that a record of the training provided to each individual must be maintained. The record must include the name of the individual, the date of training, a description of the training provided, and the means used to verify that the employee understood the training.

Recommendation 13

In developing policies and procedures for reviewing and inspecting entities' compliance with the regulations, APHIS should include steps to verify that the entities have provided annual training, including required security

training, to all individuals authorized to access select agents, and have documented the training as required.

Agency Response. In its December 2, 2005, response, APHIS stated:

APHIS agrees with this recommendation. To provide better guidance to inspectors, APHIS and CDC will document operational procedures for this phase of the inspection in the CDC/APHIS Operational Plan. These procedures will be finalized by September 30, 2006. Finalization is dependent upon receiving concurrence from CDC.

OIG Position. We cannot accept management decision for this recommendation. Although the response states that APHIS agrees with the recommendation, it does not specifically address whether APHIS will include steps in the inspections to verify that entities have provided annual training, including required security training, to all individuals having access to select agents. Also, the response does not state whether inspectors will determine if the training has been documented as required by the regulations. In addition, we cannot accept management decision for corrective action that is contingent upon receiving concurrence from CDC. In this circumstance, the recommendation must remain open until a detailed time-phased corrective action plan has been developed.

Scope and Methodology

This report presents the results of the second phase of our audit work to determine how effectively APHIS has implemented the select agent program. During the second phase of the audit, we examined registered entities' compliance with the select agent regulations and assessed APHIS' oversight of the entities. Our fieldwork was conducted at the APHIS Headquarters in Riverdale, Maryland, and at 10 judgmentally selected laboratories. The period of review was calendar year 2003 through current operations. Fieldwork was conducted during the period October 2004 through April 2005.

To accomplish our audit objectives for this second phase, we performed the following audit procedures. At APHIS Headquarters in Riverdale, Maryland, we examined select agent registration files and registered entities' biocontainment (plants)/biosafety (animals) and security plans in order to judgmentally select 10 registered entities for review. Our selection criteria included knowledge gleaned from Phase I of this audit, as well as previous audits, select agents or toxins possessed by the registered entities, geographic considerations and type of entity (e.g., commercial, non-profit, etc.). Included in our sample of 10 registered entities were 5 academic institutions; 2 commercial companies; 1 Federal laboratory; 1 State diagnostic laboratory; and, 1 non-profit research hospital. At each selected registered entity, we performed the following steps.

- Interviewed the ROs and alternate ROs to gain an understanding of each entities implementation of the select agents or toxins regulations, as well as compliance with the regulations.
- Evaluated registered entities' biocontainment (plants)/biosafety (animals) and security plan (Plan). We examined each plan for compliance with regulatory requirements including procedures for –
 - inventory control;
 - physical security;
 - personnel security and suitability;
 - accountability for select agents or toxins;
 - security training;
 - transfer of select agents or toxins;
 - response to emergencies; and
 - reporting incidents, injuries, and breaches.
- Evaluated the entities' procedures for restricting access to select agents or toxins.

- Evaluated physical security measures in place for each laboratory where select agents or toxins were stored and/or used.
- Evaluated the entities' and laboratories' inventory control procedures.
- Evaluated the entities' policies and procedures for transferring select agents or toxins.
- Evaluated the entities' policies and procedures to notify APHIS or CDC in the event of theft, loss, or release of select agents or toxins.
- Assessed the accuracy, adequacy and completeness of the records required to be kept by each RO, including –
 - Biocontainment/Biosafety and Security Plan;
 - A current list of all individuals with access to select agents or toxins;
 - Accurate and current inventory records (including select agent or toxin source and characteristic data);
 - Permits and transfer documents issued by APHIS;
 - Security records (e.g., transactions from access control systems, visitor logs); and
 - Biosafety, containment, and security incident reports.

We conducted this audit in accordance with generally accepted government auditing standards.

Exhibit A – Agency Response



DEC 2 2005

United States
Department of
Agriculture

Animal and
Plant Health
Inspection
Service

Marketing &
Regulatory
Programs Business
Services

Riverdale, MD
20737

TO: Robert W. Young
Assistant Inspector General for Audit

FROM: W. Ron DeHaven
Administrator *Kevin Shea / for*

SUBJECT: APHIS Response to OIG Report, "Evaluation of the
Implementation of the Select Agent or Toxin Regulations
(Phase II) (33601-3-AT)

Thank you for the opportunity for the Animal and Plant Health Inspection Service (APHIS) to comment on this report. We have listed each OIG recommendation and our response.

Recommendation No. 1: Re-inspect registered entities to ensure compliance with regulations regarding the security over select agents. The inspections should be done using formal written procedures to ensure consistent and thorough reviews. In our Phase I report we recommended that formal procedures be developed.

APHIS Response

Per direction from the Office of Management and Budget, APHIS must coordinate entity inspection policy with the Centers for Disease Control (CDC). To date, CDC has not agreed to total reinspection of all current registrants. Also, good regulatory policy and resource constraints dictate that we adopt a risk based reinspection policy. APHIS will reinspect a registered entity upon submission of either an amendment, which includes the use of an agent or activity of higher risk and/or work in a new area. Also, APHIS will reinspect entities when evidence suggests there is a compliance issue or when an entity has requested amendments that results in a "higher risk" level of activity. This will be effective immediately. In the event that there are no compliance issues or registration amendments, we will reinspect each no less than every two to three years consistent with the registration schedule. This combination of risk-based and regularly scheduled reinspection plan would provide sufficient security and result in most entities being reinspected within the next two years. All reinspections will be conducted under formal procedures.

Recommendation No. 2: Develop and implement written policies and procedures to ensure authorized lists are accurately and promptly updated. The procedures should

APHIS Response to OIG Report 33601-3-AT

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include requiring the entities to verify APHIS records, and either provide corrections or attest to the accuracy of the list.

APHIS Response

APHIS agrees with this recommendation. The National Select Agent Registry (NSAR) will become functional by December 30, 2006. The NSAR will contain all of the information found on the registration application documents, which include all of the authorized individuals. The Responsible Official (RO) and the Alternate Responsible Official (ARO) will have access to this system in order to update and verify the accuracy of the data. APHIS will request programming modifications that will allow notices to be sent out quarterly to entities that require verification of their Section 4B. This will be completed by December 30, 2006.

Recommendation No. 3: Develop and implement internal controls designed to prevent the release of sensitive security information associated with registered entities.

APHIS Response

APHIS agrees with this response. The NSAR will prevent accidental release of another entity's information. For those entities that are not using the NSAR to register or amend their application, a protocol will be developed that requires second party verification of any sensitive information that is sent to an entity. This protocol will be developed by March 30, 2006.

Recommendation No. 4: Provide registered entities specific guidance for performing risk assessments, including instructions for performing site-specific risk analyses. APHIS' guidance should provide advice on how to perform threat assessments and identify vulnerabilities, and suggest security measures that could help mitigate risks.

APHIS Response

APHIS agrees with this recommendation. CDC has requested that APHIS participate in a meeting on March 6-8, 2006 in order to provide better guidance to entities in the following areas: agent specific risk/threat assessment; IT and records security; risk mitigation and screening of individuals; and compliance issues and tools. The meeting, as currently planned, will include security specialists from the federal and state governments. Using the materials generated from this meeting, APHIS (and CDC) will provide guidance to entities on risk assessment by December 1, 2006. Finalization is dependent on receiving concurrence from CDC.

Recommendation No. 5: In developing policies and procedures for reviewing and inspecting entities' compliance with the regulations, APHIS should include steps to ensure registered entities base security plans on a site-specific risk analysis. Site

APHIS Response to OIG Report 33601-3-AT

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specific risk analyses should be examined to ensure that entities perform threat assessments that address its vulnerabilities. APHIS should also ensure that security plans are developed that will mitigate the risks identified and help prevent unauthorized individuals from accessing and acquiring select agents or toxins for use in terrorism. APHIS' inspection reports should conclude whether entities' security plans were based on the results of site-specific risk analyses performed in accordance with the guidance issued.

APHIS Response

APHIS agrees with this recommendation. In response to recommendation No. 4, APHIS is working with CDC to provide guidance to entities regarding the risk assessment process. Based on these guidance documents, improved guidance for inspectors will be documented in the CDC/APHIS Operational Plan. This will be completed by December 1, 2006. Finalization is dependent upon receiving concurrence from CDC.

Recommendation No. 6: In developing policies and procedures for reviewing and inspecting entities' compliance with the regulations, APHIS should include steps to verify that entities' security plans have thoroughly addressed all critical areas identified by the regulations. APHIS' inspection reports should include whether each critical area was adequately addressed.

APHIS Response

APHIS agrees with this recommendation. A check list will be developed by June 30, 2006 that the APHIS Security Specialist will use when each entity is reviewed.

Recommendation No. 7: In developing policies and procedures for reviewing and inspecting entities' compliance with the regulations, APHIS should include steps to verify that entities are conducting and documenting annual performance tests of their security plans, and are updating plans based on the results of the performance tests, drills, or exercises. APHIS' inspection reports should conclude whether their results were appropriately utilized in updating security plans.

APHIS Response

APHIS agrees with this recommendation. To provide better guidance to inspectors, APHIS and CDC will document operational procedures for review of annual drills and exercises conducted by an entity. These procedures will be finalized by September 30, 2006. Finalization is dependent upon receiving concurrence from CDC.

Recommendation No. 8: In developing policies and procedures for reviewing and inspecting entities' compliance with the regulations, APHIS should include steps to compare its list of authorized individuals with the names of the individuals having

APHIS Response to OIG Report 33601-3-AT

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access to areas with select agents. This would include an examination of the log books or other documented entries, as well as questioning researchers concerning with individuals can access the area. Inspectors should also examine the completeness and accuracy of access log books. Inspection reports should state whether security measures are adequate to restrict access to select agents only to authorized individuals.

APHIS Response:

APHIS agrees with this recommendation. To provide better guidance to inspectors, APHIS and CDC will document operational procedures that improve methods for verification of access controls used by the entity. These procedures will be finalized by September 30, 2006. Finalization is dependent upon receiving concurrence from CDC.

Recommendation No. 9: In developing policies and procedures for reviewing and inspecting entities' compliance with the regulations, APHIS should include steps to identify and examine all areas where select agents are used or stored to ensure that access to those areas are properly secured. Inspection reports should specifically identify all areas containing select agents, state whether the areas are identified in the security plan and included in the site-specific risk assessments, and conclude as to whether security for each area is adequate.

APHIS Response:

APHIS agrees with this recommendation. To provide better guidance to inspectors, APHIS and CDC will document operational procedures for this phase of the inspection in the CDC/APHIS Operational Plan. These procedures will be finalized by September 30, 2006. Finalization is dependent upon receiving concurrence from CDC.

Recommendation No. 10: APHIS should conduct an investigation into the missing access logbook at the affected entity and, based on the outcome, make a determination as to the appropriateness of the entity's registration status.

APHIS Response: APHIS agrees with this recommendation and will request that APHIS' Investigative and Enforcement Services staff conduct an investigation of this finding and submit its findings to the Associate Administrator by March 1, 2006.

Recommendation No. 11: In developing policies and procedures for reviewing and inspecting entities' compliance with the regulations, APHIS should include steps to verify that the entities have established and implemented inventory controls and perform procedures to ensure that inventory records are accurate and up to date.

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APHIS Response:

APHIS agrees with this recommendation. To provide better guidance to inspectors, APHIS and CDC will document operational procedures for this phase of the inspection in the CDC/APHIS Operational Plan. These procedures will be finalized by September 30, 2006. Finalization is dependent upon receiving concurrence from CDC.

Recommendation No. 12: For the entity with 152 vials of biological material (31 select agents, 20 non-select agents, and 101 unidentified agents), APHIS should conduct an investigation into the discrepancies, and work with the entity to determine whether the vials should be destroyed or transferred to another registered entity.

APHIS Response:

APHIS agrees with this recommendation and has investigated this finding. The entity was storing unknown agents as “select agents.” The select agent regulations do not prevent this. Thus, no violation of the regulations have occurred.

Recommendation No. 13: In developing policies and procedures for reviewing and inspecting entities’ compliance with the regulations, APHIS should include steps to verify that entities have provided annual training, including required security training, to all individuals authorized to access select agents, and have documented the training as required.

APHIS Response:

APHIS agrees with this recommendation. To provide better guidance to inspectors, APHIS and CDC will document operational procedures for this phase of the inspection in the CDC/APHIS Operational Plan. These procedures will be finalized by September 30, 2006. Finalization is dependent upon receiving concurrence from CDC.

Informational copies of this report have been distributed to:

Administrator, APHIS (9)

ATTN: Agency Liaison Officer

Government Accountability Office (1)

Office of Management and Budget (1)

Office of the Chief Financial Officer (1)

Director, Planning and Accountability Division



United States Department of Agriculture
Office of Inspector General





United States Department of Agriculture
Office of Inspector General
Washington, D.C. 20250



DATE: November 6, 2012

AUDIT
NUMBER: 33701-0001-AT

TO: Kevin Shea
Acting Administrator
Animal and Plant Health Inspection Service

ATTN: Joanne L. Munno
Deputy Administrator
Marketing Regulatory Program Business Services

FROM: Gil H. Harden
Assistant Inspector General for Audit

SUBJECT: Follow Up on APHIS' Implementation of the Select Agent or Toxin Regulations

This report presents the results of the subject audit. Your written response to the official draft, dated September 28, 2012, is included in its entirety at the end of the report. Excerpts from your response and the Office of Inspector General's (OIG) position are incorporated in the relevant Findings and Recommendations sections of the report. Based on your responses, we were able to accept management decision on Recommendations 4, 6, and 12. However, we are unable to accept management decision on Recommendations 1, 2, 3, 5, 7, 8, 9, 10, and 11. Documentation or action needed to reach management decision for these recommendations is described under the relevant OIG Position sections.

In accordance with Departmental Regulation 1720-1, please furnish a reply within 60 days, describing the corrective actions taken or planned, and timeframes for implementing the recommendations for which management decisions have not been reached. Please note that the regulation requires management decision to be reached on all recommendations within 6 months from report issuance, and final action to be taken within 1 year of each management decision to prevent being listed in the Department's annual Performance and Accountability Report. Please follow your internal agency procedures in forwarding final action correspondence to the Office of the Chief Financial Officer.

We appreciate the courtesies and cooperation extended to us by members of your staff during our audit fieldwork and subsequent discussions.

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Follow Up on APHIS' Implementation of the Select Agent or Toxin Regulations

Executive Summary

After the events of September 11, 2001, the Government took a number of steps to strengthen homeland security. *The Public Health Security and Bioterrorism Preparedness and Response Act of 2002*¹ (Public Law 107-188, signed June 12, 2002 (hereafter referred to as “the Act”)) included provisions for enhancing controls over dangerous biological agents and toxins. The Act addressed the lack of authority for the Secretary of Agriculture to regulate possession of biological agents that, through acts of bioterrorism, could have a devastating impact on the domestic agricultural economy. With passage of the Act, the Secretary of Agriculture was required to promulgate regulations to provide for the establishment and enforcement of standards and procedures governing the possession, use, and transfer of select agents or toxins, including security measures and controls to limit access to only those individuals that have a legitimate need to handle or use such agents or toxins. The Animal and Plant Health Inspection Service (APHIS) was delegated authority to administer the regulations for the Department of Agriculture.

In prior audits of APHIS' select agent program,² we found that APHIS had not established a consistent and thorough inspection structure. In response to our recommendations, APHIS established controls to ensure registered entities complied with security regulations, including enhancing its reviews of entity security plans. In addition, APHIS enhanced its inspection process by requiring inspectors to observe security procedures to verify compliance with the security plan and determine whether entities' controls were in accordance with program regulations. The primary objective of this audit was to follow up on our prior audits and assess whether APHIS' new controls are effectively ensuring that registered entities comply with regulations governing the possession, use, and transfer of select agents. We selected 7 of 59 entities that were registered to possess or use select agents to assess their compliance with select agent regulations and determine whether APHIS was effectively overseeing the select agent program at these entities.

Although APHIS has made progress in establishing controls over the select agent program since our last audit, we found that APHIS needs to strengthen its internal controls over the critical program areas related to monitoring the movement of select agents to alternate facilities, controlling access to select agents, ensuring that individuals handling select agents have up-to-date security clearances, and ensuring that responsible officials (RO) are adequately trained. Our audit discovered deficiencies in these critical areas because APHIS did not always (1) ensure effective monitoring of ongoing activities, (2) fully address identified risks, or (3) ensure effective communication within the select agent program. We found deficiencies where

¹ Title II, Subtitle B of *the Public Health Security and Bioterrorism Preparedness and Response Act of 2002* is cited as *the Agricultural Bioterrorism Protection Act of 2002*.

² *APHIS Evaluation of the Implementation of the Select Agent or Toxin Regulations, Phase I* (Audit Report 33601-0002-AT, dated June 23, 2005) and *APHIS Evaluation of the Implementation of the Select Agent or Toxin Regulations, Phase II* (Audit Report 33601-0003-AT, dated January 17, 2006).

inspector training and procedures performed did not always ensure that monitoring inspections identified program vulnerabilities. APHIS did not have adequate controls to ensure that legislatively required Department of Justice security risk assessments (SRA) for individuals possessing or using select agents were up-to-date. Finally, APHIS' lack of effective internal and external communication resulted in violations going undetected, such as (1) the transfer of select agents causing anthrax (*Bacillus anthracis*)³ and the plague (*Yersinia pestis*)⁴ to an unregistered facility and (2) access granted to personnel with expired security risk assessments to areas containing select agents at four of the seven entities we reviewed. These communication breakdowns increased the risk that select agents could be accessed by unauthorized personnel and potentially misused.

Finally, at five of the seven entities ROs or alternate ROs did not have documentation of their required biosafety or biocontainment and security training. APHIS did not require ROs or alternate ROs to have specific training related to their select agent program oversight responsibilities. Without appropriate training, ROs or alternate ROs could be providing incorrect or incomplete information to their employees, thus heightening the risk to the health of persons, plants, or animals. Additionally, all seven entities that we reviewed either did not ensure that all employees received the required training or did not maintain complete training records for their employees.

Recommendation Summary

To strengthen internal controls for monitoring program activities, addressing identified risks, and effectively communicating information about the select agent program, we recommend that APHIS revise inspection procedures to include steps for sampling and reviewing access logs; establish agency security policies and procedures for handling requests from registered entities to transfer select agents, under special circumstances; provide guidance to its registered entities to clarify the restricted access requirements; notify each registered entity to clarify that the RO must ensure that SRA renewals are timely, prior to expiration; and develop and conduct training for all ROs and alternate ROs that provides the knowledge necessary to effectively oversee the select agent program.

Agency Response

In its September 28, 2012, response to the official draft report, APHIS agreed with 3 of the 12 recommendations. Although APHIS did not agree with two of the recommendations, it proposed corrective actions that address the concerns identified by the Office of Inspector General (OIG). Excerpts from the response and OIG's position have been incorporated into the relevant sections of the report. The written response is included in its entirety at the end of the report.

³ *Bacillus anthracis* is the bacterium that causes anthrax. It is considered one of the most serious bioterrorism threats.

⁴ *Yersinia pestis* is the bacterium that causes the plague. It is considered one of the most serious bioterrorism threats.

OIG Position

The agency in their response expressed concerns that certain language in the report was unduly alarming and suggested that it should be revised or removed from the audit report. In considering management concerns, we revised certain language in the report. Further, we accept APHIS' management decision for Recommendations 4, 6, and 12, however for recommendations 1, 2, 3, 5, 7, 8, 9, 10, and 11, we were unable to reach management decision. We have provided our comments and a description of actions needed to reach management decision for each of these recommendations in the OIG Position section of the report.

Background and Objectives

Background

Biological agents and toxins that pose a severe risk to plant and animal health or to animal and plant products, such as bovine spongiform encephalopathy (BSE),⁵ are regulated by the Department of Agriculture (USDA) as “select agents or toxins” (hereafter referred to as “select agents”). *The Agricultural Bioterrorism Protection Act of 2002*⁶ (hereafter referred to as “the Act”) gives the USDA authority to designate certain plant and animal biological agents and toxins as select agents by listing them in the *Federal Register* on a biennial basis.

The Act also requires that the Secretary of Health and Human Services (HHS) establish and maintain a list of select agents that have the potential to pose a severe threat to public health and safety (public health being focused on humans instead of plants and animals). Where HHS and USDA list some of the same agents, known as overlap agents,⁷ the two departments coordinate.⁸ In USDA, the Animal and Plant Health Inspection Service (APHIS) enforces the Act, while in HHS, the Centers for Disease Control and Prevention (CDC) enforces the Act. Further, the Act requires that a national database be established to identify the names of persons, location, and identification of the select agents that are possessed, used, or transferred by the registered entities. To accomplish this, CDC established and APHIS uses the National Select Agent Registry (NSAR) database.

APHIS and CDC regulate select agents by establishing and enforcing:

- Safety procedures for the transfer of listed agents, including measures to ensure proper training and appropriate skills to handle select agents, and proper laboratory facilities to contain and dispose of select agents;
- Security measures to prevent access to select agents for use in domestic or international terrorism or for any other criminal purpose; and
- Procedures to protect public safety, animal and plant health, as well as animal and plant products, in the event of a transfer or potential transfer of select agents in violation of the established safety procedures or established safeguards and security measures.

All entities that possess, use, or transfer these select agents must register with the appropriate regulatory agency, APHIS or CDC, depending on the type of select agents the entity possesses. Entities with overlap agents may choose to register with either APHIS or CDC, but registration

⁵ BSE, widely referred to as "mad cow disease," is a chronic degenerative disease affecting the central nervous system of cattle. All infected cattle die. There is neither any treatment nor a vaccine to prevent the disease.

⁶ Title II, Subtitle B of the *Public Health Security and Bioterrorism Preparedness and Response Act of 2002* is cited as the *Agricultural Bioterrorism Protection Act of 2002*.

⁷ Overlap agents are those agents that may affect both animal and human health.

⁸ For select agents that are designated as overlap agents, CDC and APHIS are to coordinate to minimize conflicts between regulations and program activities and administrative burdens, subject to regulation by both APHIS and CDC.

with both agencies is not required. Currently,⁹ 50 entities—including government agencies, academic institutions, corporations, associations, and other legal entities—are registered with APHIS to possess, use, and transfer select agents. An entity may have multiple facilities under its purview; however, each facility is, by itself, a separate registered entity. Registered entities are defined as facilities at one physical location (such as a room, a building, or a group of buildings) where the responsible official (RO) will be able to perform all the responsibilities of the Select Agent Program.¹⁰

Each entity must designate a RO who is responsible for day-to-day program administration and compliance. The entity may also designate one or more alternate ROs, who may act in the absence of the RO. As part of the registration process, the entities' RO, the alternate RO, the entity, and the individual who owns or controls the entity,¹¹ must undergo a security risk assessment (SRA) by the Criminal Justice Information Service (CJIS) Division of the Department of Justice.¹² Moreover, all individuals who handle or use select agents must undergo an SRA by the CJIS Division.

A Federal working group¹³ established to identify and remedy potential gaps in biosecurity recommended that individuals who handle select agents undergo a renewed SRA every 3 years, as opposed to the previous timeline of every 5 years.¹⁴ APHIS and CDC accepted this recommendation and, as of June 1, 2011, began requiring individuals to have their SRA renewed every 3 years.

When an entity registers with APHIS, it submits a site-specific security plan detailing the physical security of the select agents and the laboratories that house them.¹⁵ In addition, the entity submits biosafety, biocontainment,¹⁶ and incident response plans.¹⁷ APHIS performs a

⁹ As of May 2012.

¹⁰ Registration is location specific; therefore, APHIS would classify a single corporation that owns three different facilities at distant locations handling select agents as three separate entities.

¹¹ Owning or controlling individuals undergo an SRA when applicable.

¹² The SRA is the method used by the CJIS to evaluate an individual's suitability to access select agents. Specifically, to determine whether the individual meets any of the statutory restrictors that would restrict them to access to select agents.

¹³ The working group includes the Secretaries of Defense, HHS, State, Agriculture, Transportation, and Homeland Security, or their designees.

¹⁴ Executive Order 13486, *Strengthening Laboratory Biosecurity in the United States*, January 2009, established the working group.

¹⁵ 7 *Code of Federal Regulations* (CFR) 331.11(c)(d) and 9 CFR 121.11(c)(d) require that the security plan contain, among other things, provisions for securing the area (e.g., card access, locks); provisions for controlling access to the select agents; provisions for routine cleaning, maintenance, and repairs; provisions for ensuring that all individuals with access understand and comply with the security procedures; and allow access only to individuals with access approval from APHIS.

¹⁶ 7 CFR 331.12(a)(b) and 9 CFR 121.12(a)(b) require the entity to develop and implement biosafety and/or biocontainment plans detailing the procedures to ensure biosafety and containment. The procedures must be sufficient to contain the select agent (e.g., physical structure and features of the entity, and operational and procedural safeguards).

¹⁷ 7 CFR 331.14(a)(b) and 9 CFR 121.14(a)(b) require the entity to develop and implement an incident response plan that details the entity's response procedures for events such as theft, loss, or release of select agents; security breaches; severe weather and other natural disasters; suspicious packages; and emergencies such as fire, gas leak, power outage, etc.

detailed review of the security, biosafety, biocontainment, and incident response plans and inspects the entity's facility and laboratories where select agents will be used or stored. After the initial registration is approved, APHIS performs a detailed inspection every 3 years as part of its registration renewal process. It follows up with annual compliance reviews that target certain issues, such as annual recordkeeping requirements, requirements to conduct drills and exercises, and accuracy of inventory records, based on the history or concerns with the entity. Compliance inspections are normally unannounced, and are designed to close the gap between the 3-year inspection cycles.

APHIS has 10 staff from Veterinary Services and 5 staff from Plant Protection and Quarantine (PPQ) assigned to the select agent program. Four veterinary medical officers are primarily responsible for overseeing registered entities. The PPQ director is responsible for overseeing entities that possess only plant-related select agents.

In July 2010, the President issued an executive order creating a tiered approach to classifying select agents, identifying a subset of select agents as Tier 1 agents, which are those with the greatest risk "of deliberate misuse with most significant potential for mass casualties or devastating effects to the economy, critical infrastructure, or public confidence."¹⁸ For Tier 1 agents, APHIS must revise its regulations to establish security standards specific to those agents. APHIS published the proposed list of Tier 1 agents on October 3, 2011. The executive order also created the Federal Experts Security Advisory Panel (FESAP) to make recommendations regarding biosecurity measures for the select agent program. FESAP's recommendations will be addressed during the next round of regulation revisions and FESAP will remain active through 2014.

Our 2005 review of the select agent program identified significant issues with APHIS' implementation of controls to prevent unauthorized access to select agents.¹⁹ For example, APHIS had not established policies and procedures to ensure consistent and thorough security inspections. Our subsequent review of the program in 2006 confirmed the initial findings.²⁰ Since our 2006 review, APHIS has implemented several changes to program operations in response to issues identified in prior audits, including implementing a national database of select agents, training those conducting inspections, and creating a series of checklists for conducting inspections.²¹

Objective

The objective of this audit was to follow up on our prior audits and assess whether APHIS' new controls were effectively ensuring that registered entities comply with regulations governing the possession, use, and transfer of select agents.

¹⁸ Executive Order 13546, *Optimizing the Security of Biological Select Agents and Toxins in the United States*, Section 4, July 2, 2010.

¹⁹ APHIS *Evaluation of the Implementation of the Select Agent or Toxin Regulations, Phase I* (33601-0002-AT, June 23, 2005).

²⁰ APHIS *Evaluation of the Implementation of the Select Agent or Toxin Regulations, Phase II* (33601-0003-AT, January 17, 2006).

²¹ Management decision was achieved and the agency has stated that it completed final action on all previous audit recommendations for our 2005 and 2006 reviews.

Section 1: APHIS Oversight

Finding 1: APHIS Needs to Strengthen Controls Over Critical Areas in the Select Agent Program

APHIS needs to strengthen the internal controls related to moving select agents to alternate facilities, controlling access to select agents, ensuring that individuals handling select agents have up-to-date security clearances, and ensuring that ROs are adequately trained. These internal control deficiencies occurred because APHIS did not always (1) ensure effective monitoring of ongoing activities, (2) fully address identified risks, or (3) ensure effective communication within the select agent program. As a result, there is increased risk of the misuse of select agents and the potential for serious security violations going undetected.

The *Office of Management and Budget Circular A-123*, “Management’s Responsibility for Internal Control,” states that management has a fundamental responsibility to develop and maintain effective internal control. The Government Accountability Office Standards for Internal Control in the Federal Government²² established five goals for internal controls. The first goal calls for Government agencies to establish a control environment that sets a “positive and supportive attitude toward internal control and conscientious management.” These goals also include monitoring program activities; addressing identified risks; effectively communicating information; establishing policies, procedures, techniques, and mechanisms that enforce management’s directions.

Since our prior audits, APHIS has improved its program administration. Previously, we found that APHIS had not established a consistent and thorough inspection structure. In response to our recommendations, APHIS established controls to ensure entities complied with security regulations, including enhancing its reviews of entity security plans. In addition, APHIS enhanced its inspection process by requiring inspectors to observe security procedures to verify compliance with the security plan and determine whether entities’ controls accord with program regulations. While APHIS has made progress, the executive and regulatory authorities continue to emphasize enhancing security over select agents. In July 2010, an executive order²³ instructed APHIS and CDC to increase coordination, security, and oversight for agents and toxins with the highest risk, such as those causing anthrax (*Bacillus anthracis*)²⁴ and the plague (*Yersinia pestis*).²⁵ We determined that continued efforts are needed to strengthen APHIS’ internal control environment in the areas of monitoring, risk assessment, and communication to further enhance security for these and other high risk pathogens.

²² GAO/AIMD-00-21.3.1, *Standards for Internal Control in the Federal Government*, dated November 1999, and OMB Circular A-123, *Management’s Responsibility for Internal Control*, dated December 2004.

²³ Executive Order 13546, *Optimizing the Security of Biological Select Agents and Toxins in the United States*, July 2, 2010.

²⁴ *Bacillus anthracis* is the bacterium that causes anthrax. It is considered one of the most serious bioterrorism threats.

²⁵ *Yersinia pestis* is the bacterium that causes the plague. It is considered one of the most serious bioterrorism threats.

Monitoring Ongoing Activities

APHIS has established monitoring procedures and security checklists and conducted inspector training to determine whether the programs' legislative requirements are met. However, we found that the inspector training and procedures performed did not always ensure that monitoring inspections identified program vulnerabilities. We found that APHIS' inspection procedures for monitoring registered entities did not include specific steps to review access logs to ensure that only authorized individuals were allowed access to areas with select agents. The inspection procedures also did not include steps to identify individuals whose SRAs had expired. Finally, the inspection procedures did not include steps to ensure consistency in reviewing whether entities were complying with training requirements.

For instance, while legislation clearly identifies unauthorized access to select agents as a major risk, APHIS' checklist/procedures for inspecting physical security did not require its inspectors to check entities' access logs to ensure that unauthorized individuals are not allowed in areas where select agents are stored or used. The security review checklist directs inspectors to determine whether entities "allow access only to individuals with access approval from the HHS secretary or APHIS administrator." APHIS' training material for inspectors addresses onsite observations of individuals accessing areas where select agents are stored or used during the inspection, but it does not instruct inspectors to include an examination of previous log book entries or other documented entries, such as electronic keycard access records. Three of seven entities reviewed allowed unauthorized access into areas where select agents were used or stored (see Finding 3). However, APHIS' inspections did not identify these conditions because inspection procedures did not include steps to review access logs or access privileges.²⁶ APHIS officials told us that methods for access log reviews should have been covered during the inspectors' training and that the issue should be emphasized in future training. We concluded that inspection checklists should also include steps to review access logs and access privileges.

APHIS' inspections also did not identify other deficiencies, such as individuals with expired SRAs having access to select agents (see Finding 4), and entities that did not perform required security training or adequately document it (see Finding 5). In regard to expired SRAs, the APHIS inspection guidance does not include steps to identify individuals with expired SRAs. As for training deficiencies, officials said that their intent was for inspectors to review all training records for a given period. However, the inspection guidance does not specify this requirement, nor does it instruct inspectors how to assess training records.²⁷ The checklist also does not require inspectors to document the time period covered by records reviewed during their inspection. Without documentation of the time period, APHIS is hampered in tracking and evaluating registered entities' progress in correcting identified inspection deficiencies. Also, in the event of a security incident, APHIS would be unable to definitively state whether an inspection covered a particular time period.

²⁶ Access privilege is the ability to gain access to areas where select agents are used or stored. For example, individuals who have been granted keycard access to areas where select agents are used or stored have access privileges.

²⁷ The inspection checklist states that training records should include the names, dates, descriptions, and means used to verify employees understood the training. The checklist does not indicate how many records should be reviewed or what constitutes adequate documentation of employee understanding.

Fully Addressing Identified Risks

One of the most significant risks in the select agent program is that an individual might gain access to a select agent and deliberately misuse it in a terrorist act.²⁸ A key control to mitigate this risk is included in the original legislation creating the select agent program, and requires that individuals seeking to possess or use select agents must, by law, be vetted by the Department of Justice. This requirement and process is to ensure that restricted persons are not allowed to work with select agents. Every 3 years the SRA for an individual must be renewed. We found that APHIS was not ensuring that registered entities were keeping up-to-date SRAs for individuals possessing or using select agents. Even though entities' ROs are required to ensure that the SRAs are up-to-date, APHIS was unaware that SRAs were being allowed to expire, due to inaccurate information contained in the NSAR database.²⁹ During our review at 7 registered entities, we found that SRA approval for 11 individuals at 4 entities lapsed for periods of time ranging from 14 to 478 days (see Finding 4).

APHIS does not have an effective automated system to track the SRA renewals. Instead, the agency manually compares information from the CJIS database, maintained by the Department of Justice, to data that were manually entered into the NSAR database. This manual process is more prone to errors because it relies on both manual input and comparison of data. An APHIS official told us that it is the RO's responsibility to ensure that all individuals with access to select agents have an approved SRA. However, APHIS has the responsibility to monitor the program and ensure that the registered entities are complying with select agent laws and regulations.

Effective Communication within the Select Agent Program

APHIS' lack of effective internal and external communication resulted in violations going undetected, such as the transfer of select agents to an unregistered facility and access granted to unauthorized personnel to areas containing select agents, due to expired security clearances. These communication breakdowns increased the risk that select agents could be released, misused, or diverted for terrorism. We found APHIS permitted transfers of select agents to unregistered entities due, in part, to the lack of communication about the entity's known security plan deficiencies. This occurred when the APHIS Plant Protection and Quarantine (PPQ) official approving the transfer did not communicate with the APHIS veterinary medical officer, who was responsible for overseeing the entity before signing the transfer approval document (see Finding 2).

²⁸ In a November 2, 2010, report, *Recommendations Concerning the Select Agent Program* (revised 12/20/2010 and 1/10/2011), the FESAP recommended enhancing the SRA process for the select agent program to better assess circumstances that would disqualify an individual from accessing or using select agents. In its *Report of the Working Group on Strengthening the Biosecurity of the United States*, dated October 1, 2009, a Federal working group; which includes the Secretaries of Defense, HHS, State, Agriculture, Transportation, and Homeland Security, or their designees; found that restricting select agent access to only those who have passed an SRA is critical for strengthening the United States' biosecurity. The group recommended that those with access to select agents should meet high standards of reliability, which would prevent misuse by individuals with "nefarious intent."

²⁹ NSAR is the database that APHIS and CDC use to input data regarding the select agent program; it includes the information about individuals that are authorized to use select agents.

We also found that SRAs were not up-to-date at four of the entities because the entities' ROs expected APHIS to provide them notification when the renewals were due. However, the renewal notifications were not always timely sent by APHIS because the errors and omissions in its list prevented APHIS from timely identifying individuals whose SRAs were expiring (see Finding 4).

Communication that provides accurate and reliable information is essential to ensure that those tasked with administering the select agent program at all levels understand their responsibilities and to ensure that decisions and actions affecting the program provide the best means of preventing unnecessary risks.

As noted in Finding 2, the branch chief of select agents for PPQ approved the transfer of the select agents to an unregistered entity, and not the veterinary medical officer assigned responsibility for the entity.³⁰ The branch chief obtained CDC's concurrence on the transfer, which was required because *Bacillus anthracis* (anthrax) is an overlap agent that affects both humans and animals and *Yersinia pestis* (plague) is a CDC select agent that may affect human health. Although the assigned veterinary medical officer had identified 27 deficiencies in the security and incident response plans (i.e., the incident response plan did not address how the facility would respond to events such as explosions, gas leaks, power outages, bomb threats, and suspicious packages), at the time the transfer was approved, the branch chief and CDC approved the transfer to the facility because they believed the facility was safe and secure for storing the select agents. However, the unregistered entity did not address these issues until several months after the transfer took place.

In Finding 4, an issue involved incorrect external communication provided to registered entities, which caused confusion regarding the responsibilities for monitoring and updating SRAs. We found that SRAs for all authorized persons were not up-to-date at four of the entities because APHIS was inconsistent in sending renewal notifications and did not adequately describe entity responsibilities in guidance posted on its website. APHIS and CDC maintain a NSAR website that provides information to registered entities to help them manage their select agents. Up until May 2011, under the frequently asked questions section, the site stated that APHIS or CDC will provide the RO with a list of individuals who need renewed SRAs. However, according to the program legislation, entities hold the responsibility for ensuring that SRAs are current—not APHIS. This web posting led ROs to believe that they did not need to take actions to monitor their employees' SRAs, because APHIS would do that for them. Since APHIS does not have an effective system for monitoring SRA expirations itself, the notices that it sent to ROs were often unreliable, compounding the problem.

An APHIS official told us that it is ultimately the entity's responsibility to ensure that all individuals with access to select agents have an approved SRA. In May 2011, APHIS revised its webpage to include a note stating that, "It is the [RO's] responsibility to ensure all individuals listed on the entity's registration are SRA approved." However, we believe that this clarification

³⁰ Within APHIS' select agent program, there are four veterinary medical officers, each of whom is assigned responsibility for overseeing designated registered entities possessing and using select agents affecting animals. For entities possessing only select agents affecting plants, the branch chief of select agents for PPQ would have oversight responsibility.

does not ensure that all registered entities are fully aware of their responsibilities. Many entities may not know that the site has been corrected and, since APHIS is still sending out notices, they may continue to believe that APHIS is tracking SRAs for them.

In summary, since our last audit, APHIS has established monitoring procedures and security checklists and conducted inspector training, which were all designed to ensure legislative requirements are met. However, the agency needs to improve ongoing monitoring procedures to ensure that access and movement of select agents is done in a secure environment. APHIS also needs to establish controls to ensure program risks are mitigated by monitoring whether security risk assessments are performed as required. Finally, the agency needs to provide for good communication throughout APHIS and with registered entities to ensure that decisions and actions affecting the program provide the best means of preventing unnecessary risks.

Recommendation 1

Revise inspection procedures to include steps for sampling and reviewing access logs, access privileges, and electronic entry records (if available) to ensure entities are adhering to restricted access requirements, including log book documentation requirements.

Agency Response

In its September 28, 2012, response APHIS stated:

APHIS does not concur with the recommendation. APHIS' current inspection procedures include sampling and reviewing access logs, access privileges, and electronic entry records during renewal inspections as well as annual compliance reviews. Select agent inspector training provided by APHIS specifically addresses the process to examine records and to compare those examinations with the list of authorized personnel. However, APHIS will review the inspection checklists to determine if more specificity is necessary. This review will be completed by December 3, 2012.

OIG Position

We are unable to reach management decision for this recommendation. In its response, APHIS did not provide evidence to support that its inspection procedures included sampling and reviewing access logs, access privileges, and electronic entry records. APHIS did not provide evidence showing that its inspector training specifically addressed the process to examine those records and compare those examinations with the list of authorized personnel. During our audit, we identified instances where unauthorized individuals were provided access, but such instances were not detected during APHIS' inspections. APHIS's inspection checklists, which had been provided to OIG during the audit, did not provide specific procedures for reviewing access logs, privileges, or electronic entry records. Additionally, the inspector training material provided to OIG stated that inspectors should observe individuals entering secure areas, but did not instruct the inspectors to examine previous log book entries or other documented entries such as electronic keycard access records. To reach management decision, APHIS should include steps for sampling and reviewing access logs, access privileges, and electronic entry records in its

checklists to ensure that entities are adhering to restricted access requirements, including requirements for log book documentation.

Recommendation 2

Revise the checklists and guidance used by inspectors to include (1) steps to identify evidence of required training, including what documents are needed to verify an individual's understanding of the training, and (2) the scope of an inspector's training documentation review to identify the period of time for which training records were reviewed.

Agency Response

In its September 28, 2012, response APHIS stated:

APHIS does not concur with the recommendation. Select agent inspector training provided by APHIS specifically addresses the process to examine an entity's records to ensure that the training requirements are fulfilled. APHIS inspectors review training records typically from the date of the last inspection forward by both APHIS and *** CDC on-site inspectors. APHIS will review the inspection checklists to determine if more specificity is necessary. This review will be completed by December 3, 2012.

OIG Position

We are unable to reach management decision for this recommendation. During our audit, we identified deficiencies in the training records maintained at each of the seven entities we visited. Further, the training materials provided to OIG during the audit did not identify the scope of review performed or what documents the inspectors reviewed to verify that individuals understood the training. To reach management decision, APHIS should (1) revise its inspection checklist to record the scope of the review to identify the period of time for which training records were reviewed, and (2) revise the guidance used by inspectors to identify what documents are necessary to verify an individual's understanding of training; or provide details of how its training specifically addresses the process to examine an entity's records, including identifying what documents are required to be reviewed by inspectors to verify an individual's understanding of the training, to ensure that they training requirements are fulfilled.

Recommendation 3

Develop and implement procedures to ensure that all affected parties receive communication of relevant information regarding significant decisions, such as the approval of a transfer of a select agent, before such determinations are made.

Agency Response

In its September 28, 2012, response APHIS stated:

APHIS does not concur with this recommendation. APHIS has a Standard Operating Procedure [SOP] for transfers, titled "Procedure for Processing Request to Transfer Select Agents and Toxins, APHIS/CDC Form 2," which was approved January 16, 2011. This document addresses how requests for transfers are communicated within APHIS and CDC. Part of the transfer process includes reviewing whether APHIS movement permits are valid for the recipient and sender of the select agent. If the transfer includes a CDC-only select agent or toxin, CDC must approve the request. In the transfer case cited in the OIG report, all procedures were followed correctly.

OIG Position

We are unable to reach management decision for this recommendation. The SOP cited states that if the recipient entity is not registered to possess the select agent, do not approve the transfer. In the case cited by OIG, the recipient entity did not possess a certificate of registration. Further, the SOP cited addresses communications between APHIS and CDC, not communications that occur internally within APHIS, where we cited the discrepancy. To reach management decision, APHIS should develop and implement procedures to ensure that all affected parties (both within APHIS and outside of APHIS) receive communication of relevant information regarding significant decisions, such as the approval of a transfer of a select agent, before such a determination is made.

Recommendation 4

Notify each registered entity to clarify that its RO must ensure that SRA renewals are done timely and not allowed to expire.

Agency Response

In its September 28, 2012, response APHIS stated:

APHIS does not concur with the recommendation. APHIS notifies the *** RO of the *** SRA expiration dates as a courtesy, and it is the ROs' responsibility to ensure that SRAs are renewed on time. However, the Federal Select Agent Program (FSAP) will develop a guidance document for ROs which will remind ROs that it is their responsibility to see that employee SRAs are renewed in a timely fashion. This document will be completed by December 3, 2012.

OIG Position

Although APHIS does not agree with this recommendation, its proposed corrective action to develop guidance for ROs to remind them of their responsibility to see that SRAs are renewed timely is sufficient to reach management decision. Therefore, we accept management decision for this recommendation.

Section 2: Registered Entity Compliance Issues

Finding 2: APHIS Allowed Transfers of Select Agents to Unregistered Entities Without Approved Security Plans

APHIS permitted select agent transfers to two unregistered entities that had either not yet been inspected or where inspections had revealed deficiencies in the entity's security or incident response plans.³¹ In both cases, a registered entity was relocating to a new facility that was not yet approved for the select agent program. APHIS officials explained that this occurred because the registration process for an entity can at times be lengthy if the entity has areas in the facility that are not yet complete and APHIS did not foresee circumstances where select agents might need to be transferred to a new facility owned by a registered entity before the new facility became fully registered. Therefore, APHIS had not established written policies and procedures to identify under what special circumstances, such as relocating to a new facility or temporarily transferring select agents to another location that is not registered while the entity makes emergency repairs to existing facilities, an unregistered entity may be allowed to store select agents. Because APHIS did not have assurance that the new facilities met safety and security requirements, the risk of theft, loss, or release of select agents increased.

Program regulations state that select agents may only be transferred to registered individuals or entities.³² In order to transfer select agents, the entity receiving the agents must submit a request form providing the names and quantities of the select agents or toxins being transferred, as well as the sender's name, address, and telephone number. APHIS evaluates the request and determines whether it will allow the transfer.

APHIS authorized two entities to transfer their inventories—which included *Bacillus anthracis*, *Yersinia pestis*, and BSE—to unregistered facilities that had submitted security and incident response plans, but had not yet received approval for the plans. We did note that in both cases, APHIS authorized only the storage of select agents in the unregistered facilities, but not their use.

In the first case, APHIS had identified 27 issues in the entity's incident response and security plans that needed correction. For instance, the incident response plan did not address how the facility would respond to events such as explosions, gas leaks, power outages, bomb threats, and suspicious packages.³³ However, APHIS did not communicate these deficiencies to the entity

³¹ An entity (corporation, university, or other) may have multiple facilities under its purview; however, each facility is, by itself, a separate registered entity.

³² 7 CFR 331.16, 9 CFR 121.16, and 42 CFR 73.16.

³³ Regulations require that entities have an incident response plan in place that describes an entity's response procedures for events such as bomb threats, suspicious packages, and emergencies – such as fires, gas leaks, explosions, and power outages.

until 2 months after the select agents were transferred.³⁴ The entity eventually resolved the issues, and APHIS approved the registration 7 months after the agents were transferred there.³⁵

In the second case, the entity's RO requested, on November 26, 2008, that APHIS allow the transfer of BSE to the new facility prior to registration because the lease at the old facility was expiring at the end of 2008. APHIS approved the transfer on December 2, 2008—but had yet to perform the inspection of the new facility. Additionally, APHIS did not require the entity to complete a transfer request form. Given the risks that select agents pose to human, animal, and plant health, APHIS should take steps to ensure the transfers are made only to entities that have met the safety and security requirements established in the regulations.

Overall, APHIS does not have written policies and procedures in place to allow the transfer of select agents under special circumstances. In the two cases we found, APHIS required one entity to submit a transfer request form, while instructing the other entity that a transfer request form was not required. This illustrates the need for written, formal guidance on the subject. APHIS officials acknowledged the need for policies covering select agent transfers made under special circumstances. To address this issue, we understand that APHIS is working with the CDC to develop formal procedures to allow either a temporary registration or a partial registration, such as authorizing an entity only to store a select agent in a designated room.

Recommendation 5

Establish policies and procedures for handling requests from registered entities to transfer select agents, under special circumstances, such as when an entity must relocate to facilities that are not registered with the select agent program.

Agency Response

In its September 28, 2012, response APHIS stated:

APHIS concurs with this recommendation. The FSAP will develop a section of the registration form for entities to register for storage only. FSAP will also develop guidance for inspectors and entities on the requirements for such facilities. These actions will be completed and implemented by September 30, 2013.

OIG Position

We are unable to reach management decision for this recommendation. Although we agree with APHIS' proposal to develop a section of the registration form for entities to register for storage only and develop guidance for inspectors and entities on the requirements for such facilities, APHIS does not explain how this proposal relates to the transfer of select agents, under special circumstances, to an unregistered facility. To reach management decision, APHIS needs to

³⁴ The entity transferred the select agents and toxins to the new facility on February 27, 2008; however, APHIS did not notify the entity of the deficiencies until April 17, 2008.

³⁵ APHIS authorized the transfer of the select agents on February 19, 2008; however, it approved the registration of the new facility on September 22, 2008.

explain how the registration for storage only relates to the transfer of select agents, under special circumstances, to an unregistered facility and how the guidance being developed for inspectors and entities relates to the process.

Finding 3: Entities Did Not Adhere to Access Security Requirements

Three of the seven entities we reviewed allowed unauthorized individuals unescorted access to areas registered for use or storage of select agents. In addition, one of these three entities did not maintain a logbook identifying names of unauthorized individuals who accessed areas containing select agents. This occurred because entities believed that these individuals did not have access to select agents because APHIS' guidance did not clearly define what is meant by "access" to select agents, leading entities to interpret the guidance contrary to APHIS' intent.³⁶ Although the unauthorized access instances we found did not involve direct access to select agents, the lack of compliance with access security requirements increases the risk that unauthorized individuals could acquire access and potentially misuse select agents.

Individuals accessing select agents must undergo an SRA and be approved by APHIS (hereafter referred to as "SRA approval").³⁷ Anyone without SRA approval is considered unauthorized,³⁸ and may not access select agents.³⁹ Registered entities must also maintain information about all entries into areas containing select agents, including the names, names of escorts (if applicable), and the dates and times of entry.⁴⁰

In one case, a company that was registered to work with select agents such as *Bacillus anthracis* and *Yersinia pestis*, allowed an unauthorized individual keycard access to a lab space registered for select agent use. The person in question was a scientist who worked in the same facility, but did not have SRA approval. As a result, the unauthorized scientist could enter the space registered for select agent use at any time.⁴¹ Facility officials said that select agents were not in use in the registered area when the scientist entered, and therefore they did not think this was a violation of regulations. However, this policy contradicts the company's security plan, which states that only SRA-approved persons would have unescorted access to areas where select agents are used or stored. As a result of our finding, APHIS officials conducted a review of the company and determined that it was in violation of regulations.

The two other entities in question gave maintenance workers who were not SRA approved unescorted access to areas registered for select agent use. In one case, a company, which works with highly pathogenic avian influenza,⁴² allowed maintenance workers key card access to the registered area while the facility was temporarily shut down for maintenance. The RO at the company stated that, since the facility was shut down and select agents were not in use, he did not believe that the individuals had access to select agents. However, the company's security

³⁶ APHIS officials stated their intent was that no unauthorized individuals (individuals without an approved SRA) should be allowed into any area registered for select agent use—regardless of whether the agents were present or not—unless such access is granted for a specific purpose and documented in an APHIS-approved security plan.

³⁷ 7 CFR 331.10(a) and (b) and 9 CFR 121.10(a) and (b).

³⁸ APHIS/CDC Guidance, *Select Agents and Toxins: Security Information Document*, dated March 8, 2007.

³⁹ 7 CFR 331.10(a) and 9 CFR 121.10(a).

⁴⁰ 7 CFR 331.17(a)(4) and 9 CFR 121.17(a)(4).

⁴¹ An entity must identify specific areas where select agents will be used or stored. This may include only one room of a facility, several rooms, an entire building, or multiple buildings. As such, we use the term "registered area" to identify those area(s) in which the entity is approved to use or store select agents.

⁴² Highly pathogenic *avian influenza*, also called "bird flu," is a virus that infects birds and can affect humans. It is highly contagious among birds and can result in high mortality rates among birds, especially chickens and turkeys.

plan stated that maintenance would be performed by SRA-approved individuals or unapproved individuals would be escorted. As such, the company was not complying with its own security plan.

Additionally, the entity maintained a sign-in book at the front door of the facility to document visitors; however, the book did not identify who accessed areas where select agents were used or stored, when such access occurred, or the name of that person's escort. The staff of the facility did not view this as noncompliance with regulations because they used electronic access records to document entry into areas containing select agents. However, this system does not capture when individuals without keycard access accompany individuals into areas where select agents are used. Thus, the company did not comply with select agent regulations which require a registered entity to maintain documentation that includes the name, name of escort (if applicable), date, and time of entry for all entries into spaces containing select agents.

In the second case, the company, which works with BSE, sought and received APHIS' approval to allow unescorted access by maintenance workers. However, the company did not revise its security plan to identify that it would allow unescorted access by workers who did not have SRA approval, nor to identify the additional security measures that would be implemented during the time such access was permitted. In addition, APHIS did not require the company to revise its security plan to reflect that it would allow access by these unauthorized individuals or identify what additional security measures would be implemented. The revised security plans should have reflected the circumstances under which access could occur and the additional security measures that would be in place during that time, such as removing all select agents from the area, decontaminating the area before access was granted, and restricting access to other areas registered for select agent use or storage.

In these two latter cases, an APHIS official acknowledged that the security plans should have been revised prior to allowing unescorted access by maintenance personnel. However, since there were no select agents present when the maintenance was performed and the one company had sought permission to allow unescorted individuals in the registered area, the risk relating to this access was minimal. Although one company sought APHIS' approval for unescorted maintenance (for painting) in a September 24, 2010, letter, APHIS' September 27, 2010, response approving the request did not inquire as to what maintenance procedures were included in the company's security plans or attempt to determine whether a change was needed in the company's security plan to address future maintenance needs.

These first two cases occurred because companies did not believe that the individuals had access to select agents because APHIS had not clearly defined what is meant by "access" to select agents. The regulations state that an individual has access if the individual has possession of the select agent or the "ability to gain possession" of a select agent. However, the term "ability to gain possession" is not defined. Therefore, the entities in the first two cases believed that, as long as select agents were not in use or stored in the registered area when unauthorized individuals entered, it was acceptable to allow access. However, because select agents may be brought into the registered space at any time, individuals with keycard access to these areas could potentially have access to select agents.

APHIS officials stated that their intent was that no unauthorized individuals should be allowed into any area registered for select agent use—regardless of whether the select agents were present or not—unless such access was granted for a specific purpose and documented in an APHIS-approved security plan.

Generally, we found that registered entities are not always following their approved security plans when permitting access to areas where select agents are used or stored, even though these plans were appropriately designed to comply with regulations in prohibiting access to areas where select agents were used and/or stored. To ensure that registered entities understand their responsibilities, fully comply with access requirements, and adequately secure select agents, APHIS should clarify its guidance. APHIS officials agreed that they could issue guidance to clarify access requirements.

Recommendation 6

Provide guidance to registered entities that clarifies the restricted access requirements for select agent registered space. Specifically, the guidance should (1) clearly define “access” and the meaning of “ability to gain possession,” and (2) clarify whether access is prohibited to all areas registered for select agent use, storage, and transfer, and include examples of appropriate and inappropriate access control scenarios.

Agency Response

In its September 28, 2012, response APHIS stated:

APHIS concurs with this recommendation. APHIS will clarify “access” and “ability to gain possession” in its security plan guidance document and escort policy guidance document. These documents will be revised by June 28, 2013.

OIG Position

We accept management decision for this recommendation.

Recommendation 7

Ensure that the company, which allowed the scientist who was not SRA approved, restricts access to that individual or obtains appropriate approvals to allow that individual to have access to select agent registered space.

Agency Response

In its September 28, 2012, response APHIS stated:

Shortly after OIG advised us of this incident, APHIS sent an inspection team, that also included APHIS Investigative and Enforcement Services, to review the incident.

APHIS subsequently issued a letter of warning to the entity on February 3, 2012. The entity has assured APHIS in writing that the individual no longer has access to the registered space.

OIG Position

We are unable to accept management decision for this recommendation. In the recommendation we ask that APHIS ensure that the entity has either restricted that individual's access or obtained approval to allow the individual to have access to the registered space. While we appreciate APHIS' actions in investigating the matter promptly, APHIS has not ensured that the individual no longer has access to the registered space. To reach management decision, APHIS needs to verify that the individual no longer has access to the registered space.

Recommendation 8

Require the company that allowed unapproved maintenance workers keycard access for select agent areas to revise its security plan to reflect how it provides access to registered areas for conducting maintenance activities.

Agency Response

In its September 28, 2012, response APHIS stated:

APHIS does not concur with the recommendation. In Title 9 of the *Code of Federal Regulations* (CFR) section 121.11(c) and 7 CFR 331.11(c), the select agent regulations state that entities must specify in their security plan provisions for controlling access to select agents and toxins and provisions for routine cleaning, maintenance, and repairs. In the specific instance cited above, the entity had removed select agents from the registered area; therefore, the maintenance workers did not have access to select agents. The entity's security plan properly identifies procedures for access and escort of non-SRA personnel in areas where there is the potential for access to select agents. Therefore, changes are not needed to the entity's security plan.

OIG Position

We are unable to reach management decision for this recommendation. The regulations cited by APHIS above are comprised of two distinct requirements the security plan must: (1) contain procedures for the control of access to select agents and toxins and (2) contain provisions for routine cleaning, maintenance, and repairs. We agree that the entity's security plan included both these elements. However, the entity was not conducting its cleaning, maintenance, and repairs in accordance with its written security plan. Because operating in a manner that is incongruent with its written security plan could give rise to additional security and safety risks, the security plan should be revised to reflect how the entity actually conducts its maintenance, cleaning, and repairs. This will allow APHIS to ensure that appropriate controls are in place to ensure the security of the select agents and safety of those performing the cleaning, maintenance,

and repairs. To reach management decision, APHIS needs to require the company in question to revise its security plan to reflect how it performs its cleaning, maintenance, and repair activities.

Recommendation 9

Determine whether the company that sought permission to allow unescorted access by unapproved maintenance workers continues to engage in the practice of allowing unescorted access. If so, require the company to revise its security plan to include a provision to allow unescorted maintenance workers and describe the types of additional security measures to be implemented when unescorted persons are present.

Agency Response

In its September 28, 2012, response APHIS stated:

APHIS does not concur with this Recommendation. Regulations in 9 CFR 121.11(c) and 7 CFR 331.11(c) state that entities must specify in their security plan provisions for controlling access to select agents and toxins and provisions for routine cleaning, maintenance, and repairs. In the specific instance cited above, the entity had removed select agents from the registered area; therefore, the maintenance workers did not have access to select agents. The entity's security plan properly identifies the procedures for access and escort of non-SRA personnel in areas where there is the potential for access to select agent regulations. Therefore, changes are not needed to the entity's security plan.

OIG Position

We are unable to reach management decision for this recommendation. The regulations cited by APHIS are comprised of two distinct requirements; the security plan must (1) contain procedures for the control of access to select agents and toxins and (2) contain provisions for routine cleaning, maintenance, and repairs. We agree that the entity's security plan included both these elements. However, the entity was not following the procedures in its written security plan. To reach management decision, APHIS needs to determine whether the entity is now following its written security plan. If not, the entity should be required to revise its security plan to reflect actual procedures for cleaning, maintenance, and repairs.

Finding 4: Persons with Access to Select Agents Did Not Possess Updated SRAs

Four of the seven entities we reviewed allowed individuals with expired SRAs continued access to select agents. Individuals identified by an entity as having a legitimate need to handle or use select agents must undergo an SRA by CJIS and may not access select agents unless approved. SRAs are valid for a maximum of 5 years.⁴³ While Federal regulations place the ultimate responsibility with the entity,⁴⁴ we found entity officials were not tracking when individual SRAs expired. Entity officials told us that they relied on APHIS to notify them that SRA renewals were needed. An APHIS official stated that the agency only provided the notices as a courtesy and expected entities to ensure that SRAs were timely renewed, even in the absence of notification from APHIS. However, as we discuss in Finding 1, APHIS' expectation of the entities was unclear, in that APHIS' procedures stated that it would notify the entity's RO when renewals were needed.

APHIS officials stated that the tracking process to identify expiring SRAs requires staff to manually compare information from two separate systems to create the list of expiring SRAs. Because this is a manual process, there is a higher risk of errors and omissions. In fact, we found the notifications APHIS provided to the ROs were not always accurate or timely. We identified a total of 11 SRA approvals that were not renewed or cancelled for time periods ranging from 14 to 478 days (see exhibit A for detail of lapses). We discovered this by obtaining the entities' lists of persons approved for select agent access, and then reviewing the date when each person's SRA was set to expire. Once their SRA expired, 10 of these individuals continued to have access to select agents for periods between 14 to 302 days before their SRA was successfully renewed. The other person continued to have access from the time his approval expired until 19 days later when he retired. However, the RO at this entity did not notify APHIS of the access termination until 478 days after the SRA had expired.

Because of the potential for a change in an individual's classification to a restricted category after being approved for access to select agents, an SRA must be renewed periodically to ensure that a person can still safely possess, use, and transfer select agents.⁴⁵ For instance, the SRA process restricts access for an individual convicted in any court of a crime punishable by a prison term exceeding 1 year, or an individual who has been committed to a mental institution. For the period of our review, SRA approval was valid for a maximum of 5 years,⁴⁶ after which the SRA must be renewed.⁴⁷ When an entity terminates a person's access to select agents, the RO must notify APHIS immediately and provide the reasons for termination.⁴⁸ If SRAs are not renewed in a timely manner and individuals continue to have access to select agents, it increases the risk that the select agents could be intentionally misused or diverted for unauthorized purposes.

⁴³ 7 CFR 331.10(g) and 9 CFR 121.10(g). Effective June 1, 2011, APHIS revised the maximum period of time for which an SRA is valid to 3 years.

⁴⁴ 7 CFR 331.10(a) and 7 CFR 331.9(a)(4); 9 CFR 121.10(a) and 9 CFR 121.9(a)(4); and 42 CFR 73.10(a) and 42 CFR 73.9(a)(4).

⁴⁵ *Report of the Working Group on Strengthening the Biosecurity of the United States*, dated October 1, 2009.

⁴⁶ Effective June 1, 2011, APHIS and CDC require that SRAs must be renewed every 3 years, instead of every 5 years.

⁴⁷ 7 CFR 331.10(h), 9 CFR 121.10(i), and 42 CFR 73.10(i).

⁴⁸ 7 CFR 331.10(i), 9 CFR 121.10(j), and 42 CFR 73.10(j).

SRA's are a key security measure for the select agent program. APHIS must create a reliable list to serve as the foundation of its SRA approval monitoring efforts. APHIS must also ensure that ROs accurately track their employees' SRA approvals and timely renew them before they expire. We understand APHIS is now working to automate its list compilation process to ensure accuracy, as well as more timely notification to the ROs.

Recommendation 10

Develop and implement policies and procedures for monitoring ROs to ensure the ROs are seeking timely renewals or terminations of individuals' SRA's.

Agency Response

In its September 28, 2012, response APHIS stated:

APHIS does not concur with the recommendation. APHIS will analyze the discrepancies provided by OIG to determine the reasons for possible lapses in individual's SRA's. If needed, we will develop processes to address these lapses. The analysis will be completed by December 3, 2012.

OIG Position

We are unable to accept management decision for this recommendation. Because APHIS is responsible to ensure that entities are complying with program requirements, the agency needs to monitor the ROs to ensure that they are renewing or terminating each individual's SRA, as appropriate. To reach management decision, APHIS needs to develop and implement policies and procedures for monitoring ROs to ensure that the ROs are seeking timely reviews or terminations of individuals' SRA's.

Finding 5: Responsible Officials and Employees Lacked Required Biosafety and Security Training

Five of the seven entities' ROs or alternate ROs did not have documentation of their required biosafety or biocontainment and security training. ROs and alternate ROs serve as select agent regulations experts in their respective entities, and often train their staff in safety and security measures. Although APHIS requires all individuals with access to select agents, including the RO and alternate RO, to have annual training on biosafety and security, APHIS did not require ROs or alternate ROs to have specific training related to their select agent program oversight responsibilities. The ROs and alternate ROs did not always comply with the select agent regulations in the maintenance of required training documentation to evidence training provided. Further, without appropriate training, ROs or alternate ROs could be providing incorrect or incomplete information to their employees. Additionally, all seven entities either did not ensure that all employees received the required annual training, or did not maintain complete training records for their employees, including evidence that the employees understood the training received. In 2 cases, entities did not provide training to all 58 individuals for 1 year. If training is not routinely conducted or is not understood, individuals working with select agents could develop critical knowledge gaps. These lapses in program training heighten the risk that individuals could hurt themselves or damage public, plant, or animal health if they mishandle a select agent or inadvertently cause a security breach.

Entities must provide biosafety or biocontainment and security training to each SRA-approved person before he/she can gain access to select agents, and refresher training annually thereafter.⁴⁹ Entities must also maintain records, including the date and description of the training, as well as the means used to verify that the individual understood the training (such as a quiz or test).⁵⁰ These records must be maintained for 3 years.⁵¹

Responsible Officials' Training

At five of the seven entities we visited, the RO or alternate RO did not document that they received or understood the required training in biosafety or biocontainment and security. They stated that APHIS had not provided guidance as to how ROs and alternate ROs were to meet the training requirements or how they were to document their training when they served as the subject matter expert and provided the training to other staff. Further, we noted that APHIS has not required any specific training for the ROs or alternate ROs to ensure that those responsible for implementing and overseeing the select agent programs at the registered entities have the knowledge necessary to effectively oversee the program. During our audit, we noted certain issues, which highlighted the need for training specifically focused on ensuring that ROs and alternate ROs are aware of select agent program requirements. For example, as we discussed in Finding 3, not all ROs clearly understood that only individuals with an SRA approval may have access to areas where select agents are used or stored. Additionally, as we discussed in Finding 4, ROs were relying on APHIS to notify them when an individual's SRA was due to expire, instead of monitoring that themselves and ensuring timely renewals. Without appropriate

⁴⁹ 7 CFR 331.15, 9 CFR 121.15, and 42 CFR 73.15.

⁵⁰ APHIS/CDC Guidance, *Select Agents and Toxins, Security Information Document*, March 8, 2007.

⁵¹ 7 CFR 331.17(c), 9 CFR 121.17(c), and 42 CFR 73.17(c).

training, ROs could be providing incorrect or incomplete information to their employees, thus heightening the risk to the health of persons, plants, or animals.

APHIS acknowledged that it has not issued specific training requirements for ROs. However, on October 3, 2011, APHIS issued a proposed rule that will require ROs to possess appropriate training or expertise to ensure that the entity they oversee meets the requirements of the regulations. In addition, APHIS officials stated that, as a result of our concerns, they have discussed developing training specifically for ROs to ensure that ROs are knowledgeable of select agent program requirements, but, due to other priorities, they have yet to develop the training.

Training Other Authorized Persons

All seven entities did not maintain complete training records for all approved individuals or ensure that all individuals received the required training. For example, 2 entities did not provide the required annual training to any of the 58 persons registered to work with select agents for 1 of the 3 years that we reviewed. For one of these cases, the RO stated that he did not know why training was not provided because he was not the RO during that year. At the other, the RO stated that, instead of providing formal training, the staff read the standard operating procedures; however, this did not include a procedure to ensure that the person receiving the training understood the training, which is part of the training requirements.

Generally, where entities did not have complete records to document the required training, it was because they had not retained the required records. In one instance where the entity did not maintain records for the 3-year period required by APHIS regulations, the RO stated that it was because the entity's computer system purged the training records after 12 months. At another entity where they did not require all SRA-approved individuals to attend training, the RO said that the three SRA-approved individuals that did not receive training did not routinely access select agents, or were escorted when they were in the presence of select agents. However, APHIS regulations require that all individuals, whether SRA-approved or not, receive training prior to entering areas where select agents are used or stored.

Recommendation 11

Develop and conduct training for all ROs and alternate ROs that provides the information necessary to effectively oversee the select agent program. The session should provide a method of assessing that ROs and alternate ROs understood the training.

Agency Response

In its September 28, 2012, response APHIS stated:

APHIS does not concur with this Recommendation. The FSAP held workshops on RO duties and responsibilities on November 16, 2011; May 10, 2011; June 15, 2010; August 12, 2009; and December 9, 2008. We will hold another workshop for ROs on November 16, 2012. A training requirement for ROs and alternate ROs was included in the

proposed rule published in December 2011, titled “Agricultural Bioterrorism Protection Act of 2002; Biennial Review and Republication of the Select Agent and Toxin List; Amendments to the Select Agent and Toxin Regulations.” The public comments we received did not support such a requirement. However, FSAP will develop a guidance document that describes RO responsibilities; this will be completed by December 3, 2012.

OIG Position

We are unable to reach management decision for this recommendation. Although the workshops for ROs are beneficial, as would be a guidance document, they do not provide the same level of assurance that the ROs and alternate ROs are adequately knowledgeable of select agent regulations as would specific training, especially when the training is accompanied by a method for assessing that the ROs and alternate ROs understood the training. We reviewed the 65 public comments related to the proposed rule on Regulations.gov and found that 2 of the 65 comments favored “mandatory” periodic training of personnel working with and responsible for biosafety and biosecurity. To reach management decision, APHIS should develop and conduct training for all ROs and alternate ROs to provide the information necessary to effectively oversee the select agent program. This training should include a method of assessing the ROs and alternate ROs understanding of the training.

Recommendation 12

Provide guidance to each RO re-emphasizing the requirement that biosafety and security training must be provided to and documented for all authorized individuals with access to select agents. The guidance should state that documentation of the training must include the name of the attendee, a description of the training, date of the training, and the means used to verify that the employee understood the training. The guidance should also state that these records must be maintained for 3 years.

Agency Response

In its September 28, 2012, response APHIS stated:

APHIS does not concur with this Recommendation. The current regulations in 9 CFR 121.15(c) and 7 CFR 331.15(c) already require that documentation of the training include the name of the attendee, a description of the training, date of the training, and the means used to verify that the employee understood the training. The 3-year records retention is also a requirement in 9 CFR 121.17(c) and 7 CFR 331.17(c). We will re-emphasize the training requirements in the RO guidance document that will be finalized by December 3, 2012. (This guidance document is the same document mentioned in Recommendations 4 and 11.) These requirements will also be specified in the security guidance document that will be developed by December 3, 2012.

OIG Position

Although APHIS does not agree with this recommendation, its proposed corrective action to re-emphasize the training requirements in the RO guidance document is sufficient to reach management decision. We accept management decision for this recommendation.

Scope and Methodology

This is our follow up audit to Phases I and II of APHIS' implementation of the select agent program to determine whether APHIS' new controls are effectively ensuring that registered entities are complying with governing regulations.⁵² We examined registered entities' compliance with the select agent regulations and assessed APHIS' oversight of the entities from March 2010 through January 2012.

We conducted fieldwork at APHIS Headquarters in Riverdale, Maryland, and at seven judgmentally selected registered entities,⁵³ reviewing program operations from calendar year 2007 through January 2012. We judgmentally selected 7 entities from the universe of 59 registered entities⁵⁴ that were registered as of May 2010 for review, based on knowledge from previous audits, the types of select agents possessed by entities, geographic considerations, and entity type (e.g., commercial, non-profit, etc.). We used a judgmental sample so that we could review entities with a variety of select agents and security measures. Our sample of seven consisted of one academic institution, two commercial entities, two Federal entities, one State entity, and one privately-held entity. Because we did not use a statistical sample, we cannot project our results to the universe of registered entities.

To accomplish our audit objectives, we performed the following steps at APHIS headquarters:

- Reviewed corrective actions implemented as a result of our prior audits.
- Interviewed APHIS officials from both Veterinary Services and PPQ to determine what roles Veterinary Services and PPQ have in the select agent program.
- Interviewed personnel from APHIS' Investigative and Enforcement Services to determine what role Investigative and Enforcement Services has in the select agent program.
- Interviewed APHIS officials to determine agency procedures for coordinating with the CDC for activities, such as entity registration and certification, inspection, and enforcement activities.
- Interviewed APHIS officials to determine registration, renewal, and amendment policies; inspection types; transfer policies; and theft, loss, and release policies.

⁵² *APHIS Evaluation of the Implementation of the Select Agent or Toxin Regulations, Phase I* (33601-0002-AT, June 23, 2005) and *APHIS Evaluation of the Implementation of the Select Agent or Toxin Regulations, Phase II* (33601-0003-AT, January 17, 2006).

⁵³ Our sample included 10 judgmentally selected entities, but due to budget constraints, 3 of the selected entities were eliminated from the review.

⁵⁴ The 59 registered entities consisted of 8 Federal governmental entities, 7 State governmental entities, 21 academic institutions, 21 commercial entities, and 2 private entities. As of May 2012, the number of registered entities had declined to 50 because some entities withdrew from the Select Agent Program, while others are now registered under CDC's Select Agent Program, due to a change in the select agents they process.

- Examined registration files and security, biocontainment, biosafety, and incident response plans for the seven selected entities.

At the seven selected entities, we performed the following steps:

- Interviewed the ROs and alternate ROs to gain an understanding of each entity's implementation of select agent program regulations, as well as compliance with the regulations.
- Evaluated security, biocontainment, biosafety, and incident response plans. We examined each plan to ensure it included procedures for inventory control; physical security; personnel security and suitability; accountability for select agents; security training; transfer of select agents; response to emergencies; and reporting incidents, injuries, and breaches.
- Evaluated the entities' policies and procedures for restricting access to select agents, inventory control, transferring select agents, and notifying APHIS in the event of a theft, loss, or release.
- Evaluated physical security measures in place for each laboratory where select agents were stored and/or used.
- Assessed the accuracy, adequacy, and completeness of the records required by each RO including:
 - security, biocontainment/biosafety, and incident response plans;
 - site-specific risk assessments;
 - training records;
 - authorized individuals;
 - security records (e.g., transactions from access control systems, visitor logs, etc.);
 - inventory records (including select agent source and characteristic data); and
 - transfer documents issued by APHIS or CDC.

We conducted this audit in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our audit findings and conclusions based on our audit objectives. We believe that the evidence we obtained provide a reasonable basis for our findings and conclusions based on our audit objectives.

Exhibit A: Summary of SRA Renewal Deficiencies

Exhibit A identifies the number of days that elapsed between the date that the individual's SRA expired and the date that the individual's SRA was renewed, or the date that the individual's name was submitted to APHIS to be removed from the list of approved users of select agents. The first column identifies the entity at which this was observed; the second column identifies the employee sample number; the third column provides the date the SRA expired; the fourth column identifies the date the individual's SRA was renewed and/or was removed from the list of authorized users of select agents; and the fifth and final column identifies the number of days that elapsed between the SRA expiration and SRA renewal (or removal from list of authorized users).

Entity	Individual with Expired SRA	SRA Expiration Date	Approval (A)/ Removal (R) Date	Days Lapsed
Entity 1	Employee 1	03/22/2010	08/20/2010 (A)	151
Entity 1	Employee 7	06/22/2010	09/20/2010 (A)	110
Entity 1	Employee 26	11/02/2010	11/16/2010 (A)	14
Entity 1	Employee 29	12/17/2009	08/20/2010 (A)	246
Entity 3	Employee 8	05/12/2010	09/22/2010 (A)	133
Entity 3	Employee 68	05/11/2010	09/23/2010 (A)	135
Entity 4	Employee 5	03/29/2011	04/13/2011 (A)	15
Entity 5	Employee 1	12/15/2008	04/07/2010 (R)	478
Entity 5	Employee 3	12/16/2008	10/01/2009 (A)	289
Entity 5	Employee 5	12/08/2008	09/18/2009 (A)	284
Entity 5	Employee 19	03/08/2009	01/04/2010 (A)	302

Note: Employee 1 of entity 5 was shown as an authorized user from the time his approval expired, until entity 5 requested that he be removed from the APHIS list of authorized users. Officials of the entity stated that the employee retired January 3, 2009, 19 days after his approval expired. However, the entity did not request APHIS to remove the individual from the list of authorized users until April 7, 2010.

Abbreviations

APHIS	Animal and Plant Health Inspection Service
BSE	Bovine Spongiform Encephalopathy
CDC	Centers for Disease Control and Prevention
CFR	Code of Federal Regulations
CJIS	Criminal Justice Information Service
FESAP	Federal Experts Security Advisory Panel
HHS	Health and Human Services
NSAR	National Select Agent Registry
PPQ	Plant Protection and Quarantine
RO	Responsible Official
SRA	Security Risk Assessment
USDA	Department of Agriculture

**USDA'S
ANIMAL AND PLANT HEALTH
INSPECTION SERVICE'S
RESPONSE TO AUDIT REPORT**



United States
Department of
Agriculture

Animal and Plant
Health Inspection
Service

Washington, DC
20250

MEMORANDUM

TO: Gil H. Harden
Assistant Inspector General
For Audit

September 28, 2012

FROM: Kevin Shea /s/
Acting Administrator

SUBJECT: Animal and Plant Health Inspection Service's Response and Request for Management Decisions on the Office of Inspector General (OIG) Report, "Follow-Up on Animal and Plant Health Inspection Service's Implementation of the Select Agent or Toxin Regulations" (33701-01-AT)

Thank you for the opportunity for the Animal and Plant Health Inspection Service (APHIS) to comment on this report.

APHIS is committed to protecting the health of animals and plants and their products through the effective management and implementation of the select agent and toxin regulations. In its report, OIG stated that its findings resulted in "potentially dangerous violations going undetected" or "jeopardizing the health of persons, plants or animals." We believe none of the findings uncovered dangerous violations that jeopardized the health of persons, plants, or animals. We believe that such language is unduly alarming and suggest that it should be revised or removed from the audit report.

We have addressed each Recommendation. In the majority of the Recommendations, we already have polices and/or procedures in effect that address the Recommendations. In other instances, we have included our planned corrective actions and the timeframes for implementing these actions.

Recommendation 1

Revise inspection procedures to include steps for sampling and reviewing access logs, access privileges, and electronic entry records (if available) to ensure entities are adhering to restricted access requirements, including log book documentation requirements.

APHIS Response: APHIS does not concur with this Recommendation. APHIS' current inspection procedures include sampling and reviewing access logs, access privileges, and electronic entry records during renewal inspections as well as annual



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compliance reviews. Select agent inspector training provided by APHIS specifically addresses the process to examine records and to compare those examinations with the list of authorized personnel. However, APHIS will review the inspection checklists to determine if more specificity is necessary. This review will be completed by December 3, 2012.

Recommendation 2

Revise the checklists and guidance used by inspectors to include (1) steps to identify evidence of required training, including what documents are needed to verify an individual's understanding of the training, and (2) the scope of an inspector's training documentation review to identify the period of time for which training records were reviewed.

APHIS Response: APHIS does not concur with this Recommendation. Select agent inspector training provided by APHIS specifically addresses the process to examine the entity's records to ensure that the training requirements are fulfilled. APHIS inspectors review training records typically from the date of the last inspection forward by both APHIS and Centers for Disease Control and Prevention (CDC) on-site inspectors. APHIS will review the inspection checklists to determine if more specificity is necessary. This review will be completed by December 3, 2012.

Recommendation 3

Develop and implement procedures to ensure that all affected parties receive communication of relevant information regarding significant decisions, such as the approval of a transfer of a select agent, before such determinations are made.

APHIS Response: APHIS does not concur with this Recommendation. APHIS has a Standard Operating Procedure for transfers, titled "Procedure for Processing Request to Transfer Select Agents and Toxins, APHIS/CDC Form 2," which was approved January 16, 2011. This document addresses how requests for transfers are communicated within APHIS and CDC. Part of the transfer process includes reviewing whether APHIS movement permits are valid for the recipient and sender of the select agent. If the transfer includes a CDC-only select agent or toxin, CDC must approve the request. In the transfer case cited in the OIG report, all procedures were followed correctly.

Recommendation 4

Notify each registered entity to clarify that its RO must ensure that SRA renewals are done timely and not allowed to expire.

APHIS Response: APHIS does not concur with this Recommendation. APHIS notifies the Responsible Official (RO) of the security risk assessment (SRA) expiration dates as a courtesy, and it is the ROs' responsibility to ensure that SRAs

are renewed on time. However, the Federal Select Agent Program (FSAP) will develop a guidance document for ROs which will remind ROs that it is their responsibility to see that employee SRAs are renewed in a timely fashion. This document will be completed by December 3, 2012.

Recommendation 5

Establish policies and procedures for handling requests from registered entities to transfer select agents, under special circumstances, such as when an entity must relocate, to facilities that are not registered with the select agent program.

APHIS Response: APHIS concurs with this Recommendation. The FSAP will develop a section of the registration form for entities to register for storage only. FSAP will also develop guidance for inspectors and entities on the requirements for such facilities. These actions will be completed and implemented by September 30, 2013.

Recommendation 6

Provide guidance to registered entities that clarifies the restricted access requirements for select agent registered space. Specifically, the guidance should (1) clearly define “access” and the meaning of “ability to gain possession” and (2) clarify whether access is prohibited to all areas registered for select agent use, storage, and transfer, and include examples of appropriate and inappropriate access control scenarios.

APHIS Response: APHIS concurs with this Recommendation. APHIS will clarify “access” and “ability to gain possession” in its security plan guidance document and escort policy guidance document. These documents will be revised by June 28, 2013.

Recommendation 7

Ensure that the company that allowed the scientist who was not SRA approved, restricts access to that individual or obtains appropriate approvals to allow that individual to have access to select agent registered space.

APHIS Response: Shortly after OIG advised us of this incident, APHIS sent an inspection team, that also included APHIS Investigative and Enforcement Services, to review the incident. APHIS subsequently issued a letter of warning to the entity on February 3, 2012. The entity has assured APHIS in writing that the individual no longer has access to the registered space.

Recommendation 8

Require the company that allowed unapproved maintenance workers keycard access for select agent areas to revise its security plan to reflect how it provides access to registered areas for conducting maintenance activities.

APHIS Response: APHIS does not concur with this Recommendation. In Title 9 of the *Code of Federal Regulations* (CFR) section 121.11(c) and 7 CFR 331.11(c), the select agent regulations state that entities must specify in their security plan provisions for controlling access to select agents and toxins and provisions for routine cleaning, maintenance, and repairs. In the specific instance cited above, the entity had removed select agents from the registered area; therefore, the maintenance workers did not have access to select agents. The entity's security plan properly identifies the procedures for access and escort of non-SRA personnel in areas where there is the potential for access to select agent regulations. Therefore, changes are not needed to the entity's security plan.

Recommendation 9

Determine whether the company that sought permission to allow unescorted access by unapproved maintenance workers continues to engage in the practice of allowing unescorted access. If so, require the company to revise its security plan to include a provision to allow unescorted maintenance workers and describe the types of additional security measures to be implemented when unescorted persons are present.

APHIS Response: APHIS does not concur with this Recommendation. Regulations in 9 CFR 121.11(c) and 7 CFR 331.11(c) state that entities must specify in their security plan provisions for controlling access to select agents and toxins and provisions for routine cleaning, maintenance, and repairs. In the specific instance cited above, the entity had removed select agents from the registered area; therefore, the maintenance workers did not have access to select agents. The entity's security plan properly identifies the procedures for access and escort of non-SRA personnel in areas where there is the potential for access to select agent regulations. Therefore, changes are not needed to the entity's security plan.

Recommendation 10

Develop and implement policies and procedures for monitoring ROs to ensure the ROs are seeking timely renewals or terminations of individuals' SRAs.

APHIS Response: APHIS does not concur with the Recommendation. APHIS will analyze the discrepancies provided by OIG to determine the reasons for possible lapses in individuals' SRAs. If needed, we will develop processes to address these lapses. The analysis will be completed by December 3, 2012.

Recommendation 11

Develop and conduct training for all ROs and alternate ROs that provides the information necessary to effectively oversee the select agent program. The session should provide a method of assessing that ROs and alternate ROs understood the training.

APHIS Response: APHIS does not concur with this Recommendation. The FSAP held workshops on RO duties and responsibilities on November 16, 2011; May 10, 2011; June 15, 2010; August 12, 2009; and December 9, 2008. We will hold another workshop for ROs on November 16, 2012. A training requirement for ROs and alternate ROs was included in the proposed rule published in December 2011, titled “Agricultural Bioterrorism Protection Act of 2002; Biennial Review and Republication of the Select Agent and Toxin List; Amendments to the Select Agent and Toxin Regulations.” The public comments we received did not support such a requirement. However, FSAP will develop guidance document that describes RO responsibilities; this will be completed by December 3, 2012.

Recommendation 12

Provide guidance to each RO re-emphasizing the requirement that biosafety and security training must be provided to and documented for all authorized individuals with access to select agents. The guidance should state that documentation of the training must include the name of the attendee, a description of the training, date of the training, and the means used to verify that the employee understood the training. The guidance should also state that these records must be maintained for 3 years.

APHIS Response: APHIS does not concur with this Recommendation. The current regulations in 9 CFR 121.15(c) and 7 CFR 331.15(c) already require that documentation of the training include the name of the attendee, a description of the training, date of the training, and the means used to verify that the employee understood the training. The 3-year records retention is also a requirement in 9 CFR 121.17(c) and 7 CFR 331.17(c). We will re-emphasize the training requirements in the RO guidance document that will be finalized by December 3, 2012. (This guidance document is the same document mentioned in Recommendations 4 and 11.) These requirements will also be specified in the security guidance document that will be developed by December 3, 2012.

September 2009

HIGH-CONTAINMENT LABORATORIES

National Strategy for Oversight Is Needed



GAO

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Highlights of [GAO-09-574](#), a report to congressional requesters

Why GAO Did This Study

U.S. laboratories working with dangerous biological pathogens (commonly referred to as high-containment laboratories) have proliferated in recent years. As a result, the public is concerned about the oversight of these laboratories. The deliberate or accidental release of biological pathogens can have disastrous consequences.

GAO was asked to determine (1) to what extent, and in what areas, the number of high-containment laboratories has increased in the United States, (2) which federal agency is responsible for tracking this expansion and determining the associated aggregate risks, and (3) lessons learned from highly publicized incidents at these laboratories and actions taken by the regulatory agencies.

To carry out its work, GAO surveyed and interviewed federal agency officials, (including relevant intelligence community officials), consulted with experts in microbiology, reviewed literature, conducted site visits, and analyzed incidents at high-containment laboratories.

What GAO Recommends

GAO is recommending that (1) the National Security Advisor name an entity charged with government-wide strategic evaluation of high-containment laboratories and (2) the Secretaries of Health and Human Services and Agriculture address specific oversight issues regarding high-containment laboratories. The Secretaries of Health and Human Services and Agriculture agreed with our recommendations relevant to them.

View [GAO-09-574](#) or [key components](#). For more information, contact Nancy Kingsbury at (202) 512-2700 or kingsburyn@gao.gov.

HIGH-CONTAINMENT LABORATORIES

National Strategy for Oversight Is Needed

What GAO Found

The recent expansion of high-containment laboratories in the United States began in response to the need to develop medical countermeasures after the anthrax attacks in 2001. Understandably, the expansion initially lacked a clear, governmentwide coordinated strategy. In that emergency situation, the expansion was based on individual agency perceptions of the capacity their high-containment labs required as well as the availability of congressionally approved funding. Decisions to fund the construction of high-containment labs were made by multiple federal agencies in multiple budget cycles. Federal and state agencies, academia, and the private sector considered their individual requirements, but an assessment of national needs was lacking. Even now, after more than 7 years, GAO was unable to find any projections based on a governmentwide strategic evaluation of future capacity requirements set in light of existing capacity; the numbers, location, and mission of the laboratories needed to effectively counter biothreats; and national public health goals. Such information is needed to ensure that the United States will have facilities in the right place with the right specifications.

Furthermore, since no single agency is in charge of the expansion, no one is determining the aggregate risks associated with this expansion. As a consequence, no federal agency can determine whether high-containment laboratory capacity may now meet or exceed the national need or is at a level that can be operated safely. If an agency were tasked, or a mechanism were established, with the purpose of overseeing the expansion of high-containment laboratories, it could develop a strategic plan to (1) ensure that the numbers and capabilities of potentially dangerous high-containment laboratories are no greater than necessary, (2) balance the risks and benefits of expanding such laboratories, and (3) determine the type of oversight needed.

Four highly publicized incidents in high-containment laboratories, as well as evidence in scientific literature, demonstrate that (1) while laboratory accidents are rare, they do occur, primarily due to human error or systems (management and technical operations) failure, including the failure of safety equipment and procedures, (2) insiders can pose a risk, and (3) it is difficult to control inventories of biological agents with currently available technologies. Taken as a whole, these incidents demonstrate failures of systems and procedures meant to maintain biosafety and biosecurity in high-containment laboratories. For example, they revealed the failure to comply with regulatory requirements, safety measures that were not commensurate with the level of risk to public health posed by laboratory workers and pathogens in the laboratories, and the failure to fund ongoing facility maintenance and monitor the operational effectiveness of laboratory physical infrastructure.

Oversight plays a critical role in improving biosafety and ensuring that high-containment laboratories comply with regulations. However, some aspects of the current oversight programs provided by the Departments of Health and Human Services and Agriculture are dependent upon entities monitoring themselves and reporting incidents to federal regulators. Since 2001, personnel reliability programs have been established to counter insider risks, but their cost, effectiveness, and impact has not been evaluated.

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Abbreviations

ABSL	animal biosafety level
APHL	Association of Public Health Laboratories
APHIS	Animal and Plant Health Inspection Service
BMBL	Biosafety in Microbiological and Biomedical Laboratories
BSAT	biological select agents and toxins
BSC	biosafety cabinet
BSL	biosafety level
BPRP	Biological Personnel Reliability Program
CDC	Centers for Disease Control and Prevention
Defra	Department of Environment, Food, and Rural Affairs
DHS	Department of Homeland Security
DOD	Department of Defense
DOE	Department of Energy
DOJ	Department of Justice
DOS	Department of State
DSAT	Division of Select Agents and Toxins
FBI	Federal Bureau of Investigation
FDA	Food and Drug Administration
GM	genetically modified
HHS	Department of Health and Human Services
HSE	Health and Safety Executive
IBC	institutional biosafety committee
IES	Investigative and Enforcement Services
LRN	Laboratory Response Network

NBL	National Biocontainment Laboratories
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
NSABB	National Science Advisory Board for Biosecurity
OIG	Office of Inspector General
OSHA	Occupational Safety and Health Administration
PPE	personal protective equipment
RBL	regional biocontainment laboratory
rDNA	recombinant deoxyribonucleic acid
SAPO	Specified Animal Pathogen Order
TAMU	Texas A & M University
USAMRIID	U.S. Army Medical Research Institute for Infectious Diseases
USDA	Department of Agriculture

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United States Government Accountability Office
Washington, DC 20548

September 21, 2009

Congressional Requesters

Across the United States, federal and state agencies, industries, and academic institutions are building biosafety level (BSL)-3 and BSL-4 laboratories—commonly referred to as high-containment laboratories—to research dangerous pathogens (which might accidentally or intentionally be released into the environment) and emerging infectious diseases for which risks may not be clearly understood.¹ The recent increase in the number of high-containment laboratories is primarily due to the U.S. government’s burgeoning biodefense research programs following the 2001 anthrax attacks —totaling \$1 billion annually for new research.² According to the National Institute of Allergy and Infectious Diseases (NIAID), these high-containment laboratories were needed to support its research agenda for developing medical countermeasures against biothreats. Scientific research on these dangerous pathogens and the mechanisms by which they cause disease underpins the nation’s ability to successfully combat infectious diseases and is essential to the development of new and improved diagnostics, treatments, and preventive measures for a variety of infectious diseases.

¹Some use the term high- and maximum-containment laboratories to refer to BSL-3 and BSL-4 laboratories. The terms animal biosafety level (ABSL)-3 and ABSL-4 are used for laboratories that work with animals infected with indigenous or exotic agents. The term BSL-3 Ag is used to describe laboratories where studies are conducted employing large agricultural animals. However, for purposes of this report, we are using the term high-containment laboratories to refer to all these laboratories.

²In the wake of the 2001 terrorist attacks, the National Institutes of Health (NIH) convened the Blue Ribbon Panel on Bioterrorism and Its Implications for Biomedical Research. Based on the panel’s advice, NIH developed three key documents to guide its biodefense research program; these are the NIAID Strategic Plan for Biodefense Research, the NIAID Research Agenda for Category A Agents (covering agents that pose the gravest threat to human health, such as those that cause smallpox, anthrax, botulism, and plague), and the NIAID Research Agenda for Category B and C Agents (for agents whose biological properties make them more difficult to deploy or less likely to cause widespread harm than Category A agents). The strategic plan provided a blueprint to construct three essential pillars of the biodefense research program: (1) infrastructure needed to safely conduct research on dangerous pathogens; (2) basic research on microbes and host immune defenses, which serves as the foundation for applied research; and (3) targeted, milestone-driven medical countermeasure development to create the vaccines, therapeutics, and diagnostics that will be needed in the event of a bioterror attack. To implement the biodefense agendas, Congress increased NIH appropriations for biodefense research from \$53 million in fiscal year 2001 to \$1.5 billion in fiscal year 2003 and approximately \$1.7 billion in fiscal year 2005.

In 2007, we reported on issues associated with the proliferation of high-containment laboratories in the United States, including risks posed by biosafety incidents that have occurred in the past.³ The Federal Bureau of Investigation's (FBI) allegation in August 2008 that a scientist at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) was the sole perpetrator of the 2001 anthrax attacks raised additional concerns about the possibility of insider misuse of high-containment laboratory facilities, material, and technology. The public is concerned about these laboratories because the deliberate or accidental release of biological agents can have disastrous consequences by exposing workers and the public to dangerous pathogens. Highly publicized laboratory errors and controversies about where high-containment laboratories should be located have raised questions about whether the governing framework, oversight, and standards for biosafety and biosecurity measures are adequate.⁴ In this context, you asked us to address the following questions:⁵

1. To what extent, and in what areas, has the number of high-containment laboratories increased in the United States?
2. Which federal agency is responsible for tracking the expansion of high-containment laboratories and determining the associated aggregate risks?
3. What lessons can be learned from highly publicized incidents at high-containment laboratories and actions taken by the regulatory agencies?

To answer these questions, we interviewed federal agency officials as well as experts in microbiology, reviewed literature, conducted site visits, and surveyed 12 federal agencies to determine if they have a mission to track high-containment laboratories in the United States. We also interviewed officials from relevant intelligence agencies to determine if they have a mission to determine insider risks in high-containment laboratories. The

³GAO, *High-Containment Biosafety Laboratories: Preliminary Observations on the Oversight of the Proliferation of BSL-3 and BSL-4 Laboratories in the United States*, [GAO-08-108T](#) (Washington, D.C.: Oct. 4, 2007).

⁴G.K. Gronvall et. al., "Letter to Senator Edward Kennedy and Senator Richard Burr," Center for Biosecurity, University of Pittsburgh Medical Center, March 3, 2009.

⁵The request letter contained several questions. In agreement with our requester, we revised the questions as stated.

expert panel (see appendix II) that reviewed this report comprised scientists with substantive expertise in microbiological and select agent research and the operation of high-containment laboratories.

We conducted our work from September 2005 through June 2009 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives. (See appendix I for our scope and methodology and appendix II for a list of the experts who reviewed this report.)

Background

Level of Risk in High-Containment Laboratories

In the life sciences, biosafety is a combination of the containment principles, technologies, practices, and procedures that are implemented to prevent the unintentional exposure to pathogens and toxins or their accidental release. In most countries, infectious agents are classified by risk group. Agent risk group classification emphasizes the potential risk and consequences of (1) exposure and infection for the laboratory worker or (2) the release of the agent into the environment with subsequent exposure of the general population.

Risk group classification considers aspects of a given pathogen, in particular its infectivity; mode and ease of transmission; pathogenicity and virulence (including induced morbidity and case-fatality rate); susceptibility to physical or chemical agents; and the availability or absence of countermeasures, including vaccines, therapeutic remedies, and cures. Depending on the risk group classification, research on infectious agents is to be performed in facilities offering varying levels of containment, applying different types of primary containment protection (for example, biological safety cabinets), and ensuring that appropriate practices and procedures are in place.

Biosafety Levels for Laboratories Working with Human Pathogens

In the United States, laboratories working with human pathogens are classified by the type of agents used; activities being conducted; and the risks those agents pose to laboratory personnel, the environment, and the community. The Department of Health and Human Services (HHS) has

developed and provided biosafety guidelines outlined in the manual titled *Biosafety in Microbiological and Biomedical Laboratories* (BMBL).⁶ This manual provides guidelines for work at four biosafety levels, with BSL-4 being the highest. The *NIH Guidelines for Research Involving Recombinant DNA Molecules* (NIH rDNA Guidelines)⁷ similarly describe four levels of biocontainment that closely parallel those described in the BMBL. The *NIH rDNA Guidelines* apply to all research involving recombinant DNA at institutions that receive any NIH funding for such research.

Biosafety level designations, as defined in the BMBL, refer to levels of containment rather than categories of facilities. These levels of containment requirements could change from day to day depending on the risk of the work being conducted with particular agents. For example, BSL-2 practices are recommended for diagnostic work with *B. anthracis*, but BSL-3 practices are recommended for higher-risk work with *B. anthracis*, such as aerosol challenges. Table 1 shows the different biosafety levels specified in the guidelines for laboratories working with human pathogens.

⁶Department of Health and Human Services (Washington, D.C., 2007), *Biosafety in Microbiological and Biomedical Laboratories*, 5th ed.

⁷Department of Health and Human Services, (Washington, D.C., 2002) *NIH Guidelines for Research Involving Recombinant DNA Molecules*.

Table 1: Recommended Biosafety Levels for Laboratories Working with Human Pathogens

Biosafety level	Agent	Practices	Primary barriers and safety equipment	Facilities (secondary barriers)
1	Not known to consistently cause diseases in healthy adults	Standard microbiological practices	None required	Laboratory bench and sink required
2	<ul style="list-style-type: none"> Agents associated with human disease Routes of transmission include percutaneous injury, ingestion, and mucous membrane exposure 	BSL-1 practice plus <ul style="list-style-type: none"> limited access biohazard warning signs “sharps” precaution biosafety manual defining any needed waste decontamination or medical surveillance policies 	Primary barriers: <ul style="list-style-type: none"> class I or II biosafety cabinets (BSC) or other physical containment devices used for all manipulations of agents that cause splashes or aerosols of infectious materials Personal protective equipment (PPE): <ul style="list-style-type: none"> laboratory coats, gloves, and face protection as needed 	BSL-1 plus <ul style="list-style-type: none"> autoclave^a available
3	<ul style="list-style-type: none"> Indigenous or exotic agents with potential for aerosol transmission 	BSL-2 practice plus <ul style="list-style-type: none"> controlled access decontamination of all waste decontamination of laboratory clothing before laundering baseline serum 	Primary barriers: <ul style="list-style-type: none"> class I or II BSCs or other physical containment devices used for all open manipulation of agents PPE: <ul style="list-style-type: none"> protective laboratory clothing, gloves, and respiratory protection as needed 	BSL-2 plus <ul style="list-style-type: none"> physical separation from access corridors self-closing, double-door access exhaust air not recirculated negative airflow into laboratory
4	<ul style="list-style-type: none"> Dangerous exotic agents that pose a high risk of life-threatening disease Aerosol-transmitted laboratory infections have occurred; or related agents with unknown risk of transmission 	BSL-3 practices plus <ul style="list-style-type: none"> clothing change before entering shower on exit all material decontaminated on exit from facility 	Primary barriers: <ul style="list-style-type: none"> all procedures conducted in class III BSCs or class I or II BSCs in combination with full-body, air-supplied positive pressure personnel unit 	BSL-3 plus <ul style="list-style-type: none"> separate building or isolated zone dedicated supply and exhaust, vacuum, and decontamination systems other requirements outlined in the BMBL text

Source: BMBL, 5th edition.

^aAn autoclave is a device to sterilize equipment and supplies by subjecting them to high-pressure steam at 121° C or higher.

The levels refer to a combination of laboratory practices and procedures, safety equipment, and facilities that are recommended for laboratories that conduct research on these pathogenic agents and toxins. These laboratories are to be designed, constructed, and operated to (1) prevent accidental release of infectious or hazardous agents within the laboratory and (2) protect laboratory workers and the environment external to the laboratory, including the community, from exposure to the agents.

Work in BSL-3 laboratories involves agents that may cause serious and potentially lethal infection. In some cases, vaccines or effective treatments are available. Types of agents that are typically handled in BSL-3 laboratories include *B. anthracis* (which causes anthrax), West Nile Virus, *Coxiella burnetii* (which causes Q fever), *Francisella tularensis* (which causes tularemia), and highly pathogenic avian influenza virus. Work in BSL-4 laboratories involves exotic agents that pose a high individual risk of life-threatening disease or aerosol transmission or related agents with unknown risks of transmission. Agents typically handled in BSL-4 laboratories include the Ebola virus, Marburg virus, and Variola major virus.⁸

Animal Biosafety Level Criteria for Vertebrate Animals

Just as laboratories working with human pathogens are classified by BSLs 1-4, laboratories working with naturally infected vertebrate animals are classified by animal biosafety levels (ABSL) 1-4. The four ABSLs describe facilities and practices applicable to work with animals infected with agents assigned to biosafety levels 1-4, respectively. The recommendations describe four combinations of practices, procedures, safety equipment, and facilities for experiments with animals involved in infectious disease research and other studies that may require containment. Table 2 shows the different ABSLs specified in the guidelines for laboratories working with vertebrate animals.

⁸Variola major virus, by international agreement, can only be worked on in two specific facilities in the world.

Table 2: Recommended Biosafety Levels for Activities in Which Experimentally or Naturally Infected Vertebrate Animals Are Used

ABSL	Agents	Practices	Primary barriers and safety equipment	Facilities (secondary barriers)
1	Not known to consistently cause diseases in healthy adults	Standard animal care and management practices, including appropriate medical surveillance programs	As required for normal care of each species	Standard animal facility: <ul style="list-style-type: none"> no recirculation of exhaust air directional air flow recommended hand washing sink is available
2	<ul style="list-style-type: none"> Associated with human disease Hazard: percutaneous exposure, ingestion, or mucous membrane exposure. 	ABSL-1 practice plus: <ul style="list-style-type: none"> limited access biohazard warning signs “sharps” precautions biosafety manual decontamination of all infectious wastes and animal cages prior to washing 	ABSL-1 equipment plus primary barriers: <ul style="list-style-type: none"> containment equipment appropriate for animal species Personal protective equipment (PPE) <ul style="list-style-type: none"> laboratory coats, gloves, face and respiratory protection as needed 	ABSL-1 plus: <ul style="list-style-type: none"> autoclave available hand washing sink available mechanical cage washer recommended
3	<ul style="list-style-type: none"> Indigenous or exotic agents with potential for aerosol transmission Disease may have serious health effects 	ABSL-2 practice plus: <ul style="list-style-type: none"> controlled access decontamination of clothing before laundering cages decontaminated before bedding removed disinfectant foot bath as needed 	ABSL-2 equipment plus: <ul style="list-style-type: none"> containment equipment for housing animals and cage dumping activities class I, II, or III biosafety cabinets (BSC) available for manipulative procedures (inoculation, necropsy) that may create infectious aerosols. PPEs: <ul style="list-style-type: none"> appropriate respiratory protection 	ABSL-2 facility plus: <ul style="list-style-type: none"> physical separation from access corridors self-closing, double-door access sealed penetrations sealed windows autoclave available in facility
4	<ul style="list-style-type: none"> Dangerous/exotic agents that pose high risk of life-threatening disease Aerosol transmission or related agents with unknown risk of transmission 	ABSL-3 practices plus: <ul style="list-style-type: none"> entrance through change room where personal clothing is removed and laboratory clothing is put on; shower on exiting all wastes are decontaminated before removal from the facility 	ABSL-3 equipment plus: <ul style="list-style-type: none"> maximum containment equipment (i.e., class III BSC or partial containment equipment in combination with full body, air-supplied positive-pressure personnel suit) used for all procedures and activities 	ABSL-3 facility plus: <ul style="list-style-type: none"> separate building or isolated zone dedicated supply and exhaust, vacuum, and decontamination systems other requirements outlined in the text

Legend: ABSL = animal biosafety level

Source: BMBL, 5th edition.

Agricultural Biosafety Levels

According to the BMBL, risk assessment and management guidelines for agriculture differ from human public health standards. Risk management for agricultural research is based on the potential economic impact of animal and plant morbidity and mortality, and the trade implications of disease. Worker protection is important, but greater emphasis is placed on reducing the risk of the agent escaping into the environment. Biosafety level-3 Agriculture (BSL-3Ag) is unique to agriculture because of the necessity to protect the environment from a high consequence pathogen in a situation where studies are conducted employing large agricultural animals or other similar situations in which the facility barriers serve as primary, rather than secondary, containment. BSL-3Ag facilities are specially designed, constructed, and operated at a unique containment level for research involving certain biological agents in large animal species. BSL-3Ag facilities are specifically designed to protect the environment by including almost all of the features ordinarily used for BSL-4 facilities as enhancements. All BSL-3Ag containment spaces must be designed, constructed, and certified as primary containment barriers. The Department of Agriculture's Animal and Plant Health Inspection Service (APHIS) may require enhancements beyond BSL-3/ABSL-3 when working in the laboratory or vivarium with certain veterinary agents of concern.⁹

The *NIH rDNA Guidelines* provide containment standards for research involving rDNA and animals that are of sizes or have growth requirements that preclude the use of laboratory containment.

Containment Levels for Plants

Currently, the BMBL does not provide any comparable classification levels for laboratories working with plant pathogens.

Federal Agency Involvement in High-Containment Laboratories and Related Issues

Many different federal agencies are involved with BSL-3 and BSL-4 laboratories in the United States in various capacities—they may be users, owners, regulators, or funding sources.¹⁰ Examples include the following:

⁹A vivarium is an indoor enclosure for keeping and raising living animals and plants and observing them under natural conditions.

¹⁰Some of the federal agencies, such as the Department of Commerce and the Department of Transportation, help regulate the transport of hazardous biological agents and toxins that high-containment laboratories handle.

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- The Centers for Disease Control and Prevention (CDC) has its own high-containment laboratories. The Division of Select Agents and Toxins (DSAT), located within the Coordinating Office for Terrorism Preparedness and Emergency Response at CDC, regulates federal, state, academic, commercial, and private laboratories throughout the United States that possess, use, or transfer select agents.¹¹ CDC also funds some laboratory activities carried out in state public health laboratories, commonly referred to as the Laboratory Response Network (LRN).¹²
 - The Department of Agriculture (USDA) has its own laboratories, and APHIS regulates laboratories working with select agents and toxins posing a risk to animal and plant health or animal and plant products.
 - The National Institutes of Health (NIH), working through its various institutes, funds biomedical research, some of which requires high containment laboratories. NIH has containment and biosafety requirements that apply to this and other research that it funds when the research uses recombinant deoxyribonucleic acid (rDNA) molecules. The *NIH rDNA Guidelines* provide greenhouse containment standards for rDNA-containing plants, as well as plant-associated microorganisms and small animals. NIH has its own high-containment laboratories and has funded the construction of high-containment laboratories at academic institutions.
 - The Food and Drug Administration (FDA) has its own laboratories and regulates manufacturing of biological products, some of which require high-containment laboratories.

¹¹Select agents are biological agents and toxins (1) that have the potential to pose a severe threat to public health and safety, to animal or plant health, or to animal or plant products and (2) whose possession, use, and transfer are regulated by select agent rules (7 C.F.R. Part 331, 9 C.F.R. Part 121, and 42 C.F.R. Part 73). The CDC and USDA maintain a list of select agents and toxins.

¹²The LRN was established by the Department of Health and Human Services, Centers for Disease Control and Prevention (CDC), in accordance with Presidential Decision Directive 39, which outlined national antiterrorism policies and assigned specific missions to federal departments and agencies. Through collaborative efforts involving LRN founding partners, the FBI, and the Association of Public Health Laboratories, the LRN became operational in October 1999. Its objective was to ensure an effective laboratory response to bioterrorism by helping to improve the nation's public health laboratory infrastructure. Several years later, the capacity to respond to chemical terrorism was developed.

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- The Department of Commerce regulates the export of agents and equipment that have both military and civilian uses and that are often found in high-containment laboratories.
 - The Department of Defense (DOD) has its own laboratories and funds research requiring high-containment laboratories.
 - The Department of Labor's Occupational Safety and Health Administration (OSHA) regulates and inspects private-sector employee safety and health within high-containment biological laboratories and regulates federal employee safety and health in these laboratories. However, OSHA does not have statutory responsibility for the occupational safety and health of (1) contractor employees performing work at government-owned, contractor-operated sites owned by the Department of Energy (DOE) or (2) state and local government employees.
 - The Department of State (DOS) regulates the export of agents and equipment from defense-related high-containment laboratories. DOS also maintains a listing of some high-containment laboratories as part of U.S. commitments under the Biological and Toxin Weapons Convention.
 - The Department of Justice's (DOJ) Federal Bureau of Investigation (FBI) utilizes high-containment laboratories when its forensic work involves dangerous biological agents and conducts security risk assessments for the DSAT and APHIS select agent programs.
 - The Department of Homeland Security (DHS) has its own high-containment laboratories and funds a variety of research requiring high-containment laboratories.
 - The Department of Energy (DOE) has several BSL-3 laboratories doing research to develop detection and response systems to improve preparedness for a biological attack.
 - The Department of the Interior has its own BSL-3 laboratories for work with infectious animal diseases.
 - The Department of Veterans Affairs has BSL-3 laboratories for diagnostic and research purposes.
 - The Environmental Protection Agency (EPA) has its own BSL-3 laboratories and also coordinates the use of various academic, state, and commercial high-containment laboratories nationwide as part of its

emergency response mission (eLRN, environmental laboratory Response Network).

Laws, Regulations, and Guidance Pertinent to High-Containment Laboratories

Currently, no U.S. laws provide for federal government oversight of all high-containment laboratories. However, laws regulating the use, possession, and transfer of select agents and toxins impose requirements on entities with high-containment laboratories that work with these agents.¹³ The following is a short summary of pertinent laws, regulations, and guidance.

Pertinent Laws

Following the Oklahoma City bombing in 1995, Congress passed the Antiterrorism and Effective Death Penalty Act of 1996 to deter terrorism, among other reasons.¹⁴ Section 511 of title V of this act gave authority to the HHS Secretary to regulate the transfer, between laboratories, of certain biological agents and toxins. It directed the Secretary to promulgate regulations identifying a list of biological agents and toxins—called select agents—that have the potential to pose a severe threat to public health and safety, providing procedures governing the transfer of those agents, and establishing safeguards to prevent unauthorized access to those agents for purposes of terrorism or other criminal activities. In response to this act, the HHS Secretary established the select agent program within the CDC.

In reaction to the September 11, 2001, terrorist attacks and the subsequent anthrax incidents, Congress passed several laws to combat terrorism (to prevent theft, unauthorized access, or illegal use) and, in doing so, significantly strengthened the oversight and use of select agents. The USA PATRIOT Act¹⁵ made it a criminal offense for certain restricted persons—including some foreign aliens, persons with criminal records, and those with mental defects—to transport or receive select agents. The act also made it a criminal offense for any individual to knowingly possess any biological agent, toxin, or delivery system in type or quantity not justified by a peaceful purpose. Subsequently, Congress passed the Public Health

¹³Other laws regulate the transfer of various non-select agents that could originate in or be sent to high-containment laboratories. We do not discuss these regulations as they are not directly pertinent to high-containment laboratories.

¹⁴Pub. L. No. 104-132, 110 Stat. 1214, 1284 (April 24, 1996).

¹⁵United and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism Act of 2001, Pub. L. No. 107-56, 115 Stat. 271, 386 (Oct. 26, 2001).

Security and Bioterrorism Preparedness and Response Act of 2002 (Bioterrorism Act),¹⁶ which (1) expanded the select agent program to include not only the regulation of the transfer but also the use and possession of select agents and (2) increased safeguards and security requirements.

The Bioterrorism Act expanded the select agent program by

- granting comparable regulatory authorities to USDA for biological agents and toxins that present a severe threat to plant or animal health or plant or animal products;¹⁷
- requiring coordination/concurrence between USDA and HHS on select agents and toxins regulated by both agencies (“overlap” agents and toxins);
- requiring the Secretaries of USDA and HHS to establish and maintain a list of each biological agent and toxin (select agent and toxin) that has the potential to pose a severe threat to public health and safety, animal or plant health, or animal or plant products and directing the Secretaries of HHS and Agriculture to biennially review and republish the select agent list, making revisions as appropriate to protect the public;
- requiring the Secretaries by regulation to provide for registration of facilities for the possession, use, and transfer of select agents and toxins, not just for those facilities sending or receiving select agents;
- requiring the Attorney General (delegated to the FBI’s Criminal Justice Information Services Division) to check criminal, immigration, national security, and other electronic databases with information submitted in the registration process for all individuals and nongovernmental entities to determine if the registrant is a restricted person as defined in the USA PATRIOT Act or has been reasonably suspected by federal law enforcement or intelligence agencies of committing a federal crime of terrorism or having known involvement in an organization that engages in terrorism or is an agent of a foreign power (this is called a security risk assessment);

¹⁶Pub. L. No. 107-188, 116 Stat. 594, 637-662 (June 12, 2002).

¹⁷Subtitle B, of title II, of the Bioterrorism Act provides regulatory authority over select agents and toxins to the Secretary of Agriculture. This subtitle is cited as the Agricultural Bioterrorism Protection Act of 2002 (Agricultural Bioterrorism Act).

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- requiring the Secretaries to establish a national database that includes the names and locations of registered entities; the lists of agents and toxins such entities possess, use, or transfer; and information regarding the characterizations of such agents and toxins;
 - requiring the Secretaries to promulgate regulations that include safeguard and security requirements for persons possessing, using, or transferring a select agent or toxin commensurate with the risk such an agent or toxin poses to public, animal, and plant health and safety, including required notification to the Secretaries and law enforcement agencies of theft, loss, or release of a listed agent or toxin; and
 - establishing civil money penalties for persons violating the regulations and additional criminal penalties for knowingly possessing a select agent or toxin without registering it or knowingly transferring a select agent or toxin to an unregistered person.

(See appendix III for the list of select agents and toxins as of November 11, 2008.)

Pertinent Regulations and Guidance

Select Agent Program Regulations

HHS originally established the select agent program within CDC in response to the Antiterrorism and Effective Death Penalty Act of 1996. Before the select agent program was created, CDC regulated only the importation of etiologic agents. CDC published regulations governing the select agent program that became effective on April 15, 1997. These regulations provided additional requirements for facilities transferring or receiving select agents and specifically (1) established a list of select agents that have the potential to pose a severe threat to public health and safety, (2) required registration of facilities before the domestic transfer of select agents can occur, and (3) developed procedures to document the transfer of agents.¹⁸

Subsequently, the Bioterrorism Act strengthened HHS's authority to regulate facilities and individuals that possessed biological agents and toxins that pose a severe threat to public health and safety, and the Agricultural Bioterrorism Act granted comparable authority to the USDA to establish a parallel set of requirements for facilities and individuals that handle agents and toxins that pose a severe threat to animal or plant

¹⁸61 Fed. Reg. 55190 (Oct. 24, 1996).

health or animal or plant products. USDA delegated its authority to the Animal and Plant Health Inspection Service (APHIS). Both CDC and APHIS issued similar regulations governing the select agent program; these regulations became effective on April 18, 2005.¹⁹ CDC issued regulations for select agents posing a threat to public health and safety. APHIS issued separate but largely identical regulations for select agents posing a threat to plants and animals. CDC and APHIS share oversight/registration responsibilities for overlap select agents that pose threats to both public health and animal health and animal products.

In developing a list of select agents and toxins that have the potential to pose a severe threat to public health and safety, the HHS Secretary was required by the Bioterrorism Act to consider the criteria listed below. The Secretary directed the CDC to convene an interagency working group to determine which biological agents and toxins required regulation based on the following criteria:

- the effect on human health of exposure to the agent or toxin;
- the degree of contagiousness of the agent or toxin 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 any illness resulting from infection by the agent or toxin; and
- any other criteria, including the needs of children or other vulnerable populations, that the Secretary considers appropriate.

Similarly, the Agricultural Bioterrorism Act required the USDA Secretary (delegated to APHIS) to consider the following criteria when selecting biological agents to be included in the list of select agents that pose a severe threat to animal or plant health or animal or plant products:

- the effect of exposure to the agent or toxin on animal or plant health and on the production and marketability of animal or plant products;
- the pathogenicity of the agent or the toxicity of the toxin and the methods by which the agent or toxin is transferred to animals and plants;

¹⁹42 C.F.R. Part 73 (CDC); 7 C.F.R. Part 331 (APHIS-plant); 9 C.F.R. Part 121 (APHIS-animal).

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- the availability and effectiveness of pharmacotherapies and prophylaxis to treat and prevent any illness caused by an agent or toxin; and
 - any other criteria that the Secretary considers appropriate to protect animal or plant health, or animal or plant products.

Individuals and entities are required to register with CDC or APHIS prior to possessing, using, or transferring any select agents or toxins. Prior to registering, entities must designate a responsible official who has the authority and responsibility to act on behalf of the entity. Receiving a certificate of registration from the HHS Secretary or the Administrator of APHIS is contingent on CDC's or APHIS's review of the application package (APHIS/CDC Form 1) and the security risk assessment conducted by the FBI (composed of database checks and consisting of a report of criminal convictions and involuntary commitments greater than 30 days only) on the individual or nongovernmental entity (federal, state, or local governmental entities are exempt), the responsible official, and any individual who owns or controls the nongovernmental entity. Registration may also be contingent upon inspection of the facility. Submission of additional information—such as a biosecurity, biosafety,²⁰ or incident response plan—is required prior to receiving a certificate of registration. Registration is valid for one physical location and for a maximum of 3 years.

For facilities registered with CDC or APHIS that possess, use, or transfer select agents, the regulations require the following:

1. All individuals in the facility needing access to select agents and toxins must be approved by the Administrator of APHIS or the HHS Secretary following a security risk assessment by the FBI prior to having access (access approval is valid for 5 years).
2. The facility must develop and implement a written security plan sufficient to safeguard the select agent or toxin against unauthorized access, theft, loss, or release.

²⁰The terms biosafety and biosecurity are sometimes used interchangeably; however, they are different. In this report, biosafety refers to practices employed to lower the risk of accidental release of dangerous pathogens in the laboratory or environmental release from the laboratory, while biosecurity refers to steps taken to secure pathogens from theft, unauthorized access, or illegal use.

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3. The facility must develop and implement a written biosafety plan commensurate with the risk of the agent or toxin; the plan must contain sufficient information on biosafety and containment procedures.
 4. The facility must develop and implement a written incident response plan that fully describes the facility's response procedures for the theft, loss, or release of a select agent or toxin; inventory discrepancies; security breaches; severe weather; workplace violence; bomb threats; suspicious packages; and other possible emergencies at the facility.
 5. The facility must provide training on biosafety and security to individuals with access to select agents and to individuals not approved for access who will work in or visit areas where select agents or toxins are handled and stored.
 6. The facility must maintain records relating to the activities covered by the select agent regulations.
 7. The facility must immediately notify CDC or APHIS and appropriate federal, state, or local law enforcement agencies upon discovering a theft or loss of a select agent or toxin, and notify CDC or APHIS upon discovering the release of a select agent or toxin.

As a matter of policy, CDC or APHIS inspects the premises and records of applicants, including a review of all required plans, before issuing the initial certificate of registration to ensure that the entity is compliant with the select agent regulations. Also, CDC and APHIS must be allowed to inspect, without prior notification, any facility where select agents or toxins are possessed, used, or transferred. CDC and APHIS perform site visits in cases where an entity may be adding a select agent or toxin, new laboratory facility, or new procedure that requires verification of the entity's biosafety plans and procedures. Other inspections performed by CDC and APHIS include follow-up inspections based on observations from audits performed by federal partners, compliance inspections, and investigations of reported incidents that may have involved biosafety or security concerns that could affect public, animal, and plant health and safety. CDC and APHIS use specific checklists to guide their inspections. CDC and APHIS developed these checklists from the select agent regulations and the BMBL, and they are available at www.selectagents.gov. The BMBL has become the code of practice for laboratory principles, practices, and procedures.

If CDC or APHIS discovers possible violations of the select agent regulations, several types of enforcement actions may occur:

- **Administrative actions:** CDC and APHIS may deny an application or suspend or revoke a registered entity's certificate of registration if the individual or entity, responsible official, or owner of the entity is reasonably suspected of criminal violations or does not comply with the select agent regulations or if denial, suspension, or revocation is necessary to protect public, animal, or plant health and safety. A suspension can be for all select agent work at a registered entity or be specific to particular agents.
- **Civil Money Penalties or Criminal Enforcement:** CDC refers possible violations of the select agent regulations to the HHS Office of Inspector General (OIG). The HHS-OIG can levy civil money penalties (for an individual, up to \$250,000 for each violation and, for an entity, up to \$500,000 for each violation) or recommend criminal enforcement (imprisonment for up to 5 years, a fine, or both). As of April 29, 2009, CDC's DSAT had referred 48 entities to the HHS-OIG for violating select agent regulations. HHS-OIG had levied \$1,997,000 in civil money penalties against 13 of these entities. Information regarding these entities can be found on the following Web sites: http://oig.hhs.gov/fraud/enforcement/cmp/agents_toxins.asp and http://oig.hhs.gov/fraud/enforcement/cmp/agents_toxins_archive.asp. Also, the agricultural select agent program relies on APHIS' own investigative unit, USDA Marketing and Regulatory Programs—Investigative and Enforcement Services (IES), for initial investigations of potential select agent violations. Like the HHS-OIG, IES can levy civil money penalties or recommend criminal enforcement. IES refers potential criminal violations to USDA's OIG. From 2002—when APHIS first became involved with select agents—until May 7, 2009, the agricultural select agent program referred 39 entities or unregistered persons to IES for potential violations of the select agent regulations. USDA has levied \$547,500 in civil money penalties against nine of these entities or unregistered persons. USDA does not publish information on select agent investigations or the results of these investigations.
- **Referral to DOJ:** DSAT or APHIS can refer possible criminal violations involving select agents to DOJ for further investigation or prosecution.

Pertinent Guidelines

The laws and regulations discussed above provide requirements for individuals and entities possessing, using, or transferring select agents and toxins but do not apply universally to high-containment laboratories. However, guidance for operating high-containment laboratories that is not legally mandatory is available. Pertinent guidance includes HHS's BMBL manual and the *NIH Guidelines for Research Involving Recombinant DNA Molecules*.

HHS's BMBL Manual: The BMBL, prepared by NIH and CDC, categorizes laboratories on four biosafety levels (BSL) based on risk criteria, with BSL-4 laboratories being utilized for the study of agents that pose the highest threat risk to human health and safety. The BMBL describes a code of practice for biosafety and biocontainment in microbiological, biomedical, and clinical laboratories. The BMBL serves as the primary recognized source of guidance on the safe practices, safety equipment, and facility containment needed to work with infectious agents. The first publication was in 1984, and the most recent (5th edition) was published electronically in 2007. The select agent regulations reference the BMBL as a document to consider when entities are developing their written biosafety plans. Even though the BMBL is issued as a guidance document, DSAT and APHIS have incorporated certain elements of it into their inspection checklists as a requirement of the select agent program.

The BMBL states that (1) biosafety procedures must be incorporated into the laboratory's standard operating procedures or biosafety manual, (2) personnel must be advised of special hazards and are required to read and follow instructions on practices and procedures, and (3) personnel must receive training on the potential hazards associated with the work and the necessary precautions to prevent exposure. Further, the BMBL (5th edition) provides guidance on biosecurity, such as methods of controlling access to areas where agents are used or stored. The BMBL also states that a plan must be in place for informing police, fire, and other emergency responders concerning the type of biological materials in use in the laboratory areas.

NIH Guidelines for Research Involving Recombinant DNA Molecules: Some of the work in BSL-3 and BSL-4 laboratories in the United States involves rDNA, and the standards and procedures for

research involving rDNA are set by the *NIH Guidelines for Research Involving Recombinant DNA Molecules* (NIH rDNA Guidelines).²¹ Institutions must follow these guidelines when they receive NIH funding for work with rDNA. The guidelines include the requirement to establish an institutional biosafety committee (IBC), which is responsible for (1) reviewing rDNA research conducted at or sponsored by the institution for compliance with the *NIH rDNA Guidelines* and (2) reviewing categories of research as delineated in the *NIH rDNA Guidelines*. IBCs also periodically review ongoing rDNA research to ensure continued compliance with the guidelines. While the guidelines are only mandatory for those institutions receiving NIH funding, they have become generally accepted standards for safe working practice in this area of research and are followed voluntarily by many companies and other institutions not otherwise subject to their requirements.

The Number of BSL-4 and BSL-3 Laboratories and Their Workforce Are Increasing in Different Sectors throughout the United States

Since 2001, the number of BSL-4 and BSL-3 laboratories in the United States has increased, and this expansion has taken place across federal, state, academic, and private sectors and throughout the United States. Federal officials and experts believe that while the number of BSL-4 laboratories in the United States is known, the number of BSL-3 laboratories is unknown. Information about the number, location, activities, and ownership is available for high-containment laboratories that are registered with the DSAT or APHIS select agent programs but not for those outside the program.

A number of issues are associated with determining the overall number of BSL-3 and BSL-4 laboratories. In our discussions with federal agency officials and experts and in our review of the literature, we found that the total number depended upon how the question was phrased. While data were generally available on the number of facilities or sites that contained a BSL-3 or BSL-4 laboratory, the precise number of independent rooms within those facilities qualifying as BSL-3 or BSL-4 laboratories was not generally specified. Some facilities contain more than one actual laboratory. For example, while CDC has two facilities with BSL-4 capacity, one of the facilities actually contains two separate BSL-4 laboratories, while the other has four separate BSL-4 laboratories. These officials and

²¹In the context of the *NIH rDNA Guidelines*, recombinant DNA molecules are defined as either (1) molecules that are constructed outside living cells by joining natural or synthetic DNA segments to DNA molecules that can replicate in a living cell or (2) molecules that result from the replication of those described in (1) above.

experts also told us that counting the number of laboratories is problematic because the definition of the term “laboratory” varies. A more meaningful measure is determining the net square footage of working BSL-4 space. However, this information is often not available. In addition, there also are methodological issues associated with determining whether a laboratory is operational or not.

The expansion of high-containment laboratories in the United States began in response to the emergency situation resulting from the anthrax attacks in 2001. Understandably, the expansion initially lacked a clear, governmentwide coordinated strategy. In that emergency situation, the expansion was based on the perceptions of individual agencies about the capacity required for their high-containment laboratory activities as well as the availability of congressionally approved funding. Decisions to fund the construction of high-containment laboratories were made by multiple federal agencies in multiple budget cycles. Federal and state agencies, academia, and the private sector considered their individual requirements, but a robust assessment of national needs was lacking. Since each agency has a different mission, an assessment of needs, by definition, is at the discretion of the agency. We have not found any national research agenda linking all these agencies that would have allowed for such a national needs assessment. Even now, after more than 7 years, we have not been able to find any detailed projections based on a governmentwide strategic evaluation of future capacity requirements in light of existing capacity; the numbers, location, and mission of the laboratories needed to effectively counter biotreats; and national public health goals. Without this information, there is little assurance of having facilities in the right places with the right specifications to meet a governmentwide strategy.

The Number of BSL-4 Laboratories Is Increasing in Some Sectors

For most of the past 50 years, there were only two entities²² with BSL-4 laboratories in the United States: federal laboratories at USAMRIID at Fort Detrick, Maryland, and at the CDC in Atlanta, Georgia. Between 1990 and 2000, three new BSL-4 laboratories were built: (1) the first BSL-4 university

²²An entity is defined in the select agent regulations as any government agency (federal, state, or local), academic institution, corporation, company, partnership, society, association, firm, sole proprietorship, or other legal body. A private entity is a company whose shares are not traded on the open market, as a commercial entity's are.

laboratory (a glovebox, rather than a conventional laboratory)²³ at Georgia State University in Atlanta; (2) the University of Texas Medical Branch (UTMB) Robert E. Shope BSL-4 laboratory in Galveston, Texas; and (3) the Southwest Foundation for Biomedical Research, a privately funded laboratory in San Antonio, Texas. These entities were registered with CDC prior to 2004. In 2004, these entities registered their facilities with DSAT under the select agent regulations.²⁴ As of June 2009, two new BSL-4 laboratories became operational: CDC Emerging Infectious Diseases laboratory in Atlanta, Georgia, and NIAID Rocky Mountain laboratory in Hamilton, Montana. To date, there are seven operational BSL-4 laboratories in the United States.

Table 3 shows the number of entities with BSL-4 laboratories by calendar year and sector.

Table 3: Entities Registered with DSAT That Maintain BSL-4 Laboratories, by Calendar Year and Sector

Year	Total number of entities	Number of BSL-4 laboratories by sector				
		Federal government	State/local government	Academic	Private (nonprofit)	Commercial (for profit)
2004	5	2	0	2	1	0
2005	5	2	0	2	1	0
2006	5	2	0	2	1	0
2007	5	2	0	2	1	0
2008	5	2	0	2	1	0
2009	7	4	0	2	1	0

Source: CDC select agent program as of June 2009.

Note: All six entities in the United States with operational BSL-4 laboratories are registered with DSAT; none are registered with APHIS. One entity has two BSL-4 laboratories.

Since the anthrax attacks in 2001, seven new BSL-4 facilities are in the planning, construction, or commissioning stage. Four of these facilities are

²³ A glovebox (or glove box) is a sealed container that is designed to allow one to manipulate objects while being in a different atmosphere from the object. Built into the sides of the glovebox are two gloves arranged in such a way that the user can place his or her hands into the gloves and perform tasks inside the box without breaking the seal or allowing potential injury. Part or all of the box is usually transparent to allow the user to see what is being manipulated.

²⁴ Although the select agent regulations were not finalized until 2005, interim final rules required registration in 2003.

in the federal sector, two are in the academic sector, and one is in the state/local government sector.

The following are the BSL-4 facilities in the planning, construction, or commissioning stage in the federal sector:

- (1) NIAID Integrated Research Facility, Fort Detrick, Maryland;
- (2) DHS National Biodefense Analysis and Countermeasure Center, Fort Detrick, Maryland;
- (3) DHS National Bio- and Agro-Defense Facility (NBAF), Manhattan, Kansas; and
- (4) DOD USAMRIID Recapitalization, Fort Detrick, Maryland. This new BSL-4 laboratory will replace the existing USAMRIID laboratory.

The following BSL-4 facilities are in the planning or construction stage in the academic sector and are funded by NIAID:

- (5) National Biocontainment Laboratory (NBL) at Boston University, Boston, Massachusetts, and
- (6) NBL at the University of Texas Medical Branch, Galveston, Texas.

One BSL-4 facility is being built in the state/local government sector to identify and characterize highly infectious emerging diseases that pose a threat to public health:

- (7) Virginia Division of Consolidated Laboratory Services, Richmond, Virginia.²⁵

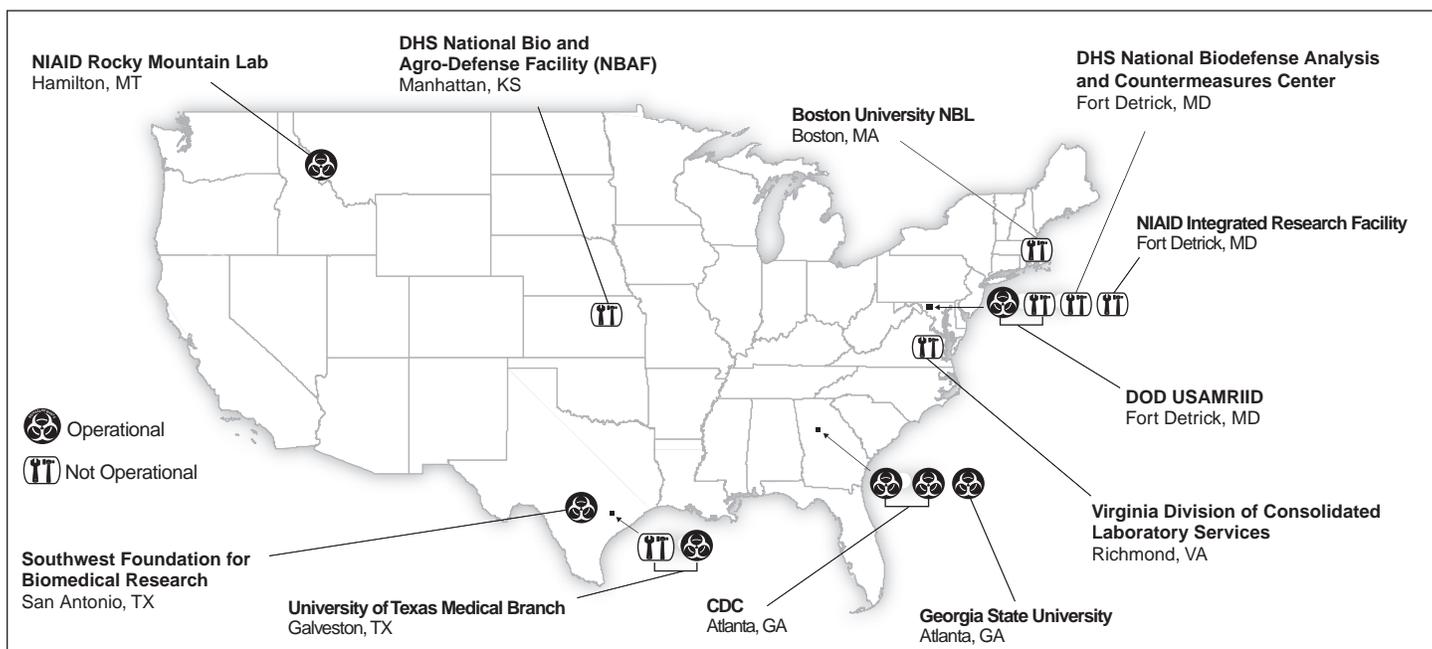
The total number of BSL-4 laboratories will increase from 7 to 13 when these laboratories become operational.²⁶ The locations of the BSL-4

²⁵According to CDC, while this laboratory is being built as a BSL-4 laboratory, it will operate as a BSL-3 laboratory.

²⁶The 7 BSL-4 laboratories that are operational as of 2009 and the 7 new facilities that are not yet operational total 14. However, the new USAMRIID Recapitalization Laboratory will replace an existing facility at Ft. Detrick, making the total 13. Figure 1, however, includes both the new and existing USAMRIID facilities since it shows both operational and nonoperational laboratories as of June 2009.

laboratories that are currently registered, under construction, or in the planning stage are shown in figure 1.

Figure 1: Entities Registered with DSAT That Maintain BSL-4 Laboratories, by Calendar Year and Sector



Source: GAO design based on NIAID information. Art Explosion (map), open sources.

Note: The figure show 14 laboratories rather than 13 because the USAMRIID Recapitalization Laboratory at Ft. Detrick is shown along with the currently operational laboratory that it will eventually replace.

CDC officials told us that the enormous cost of construction would preclude operators from building a BSL-4 laboratory unless they were going to work with one or more of the select agents that require BSL-4 level containment. Based on this reasoning, these officials believe that they know all existing operational BSL-4 laboratories in the United States because these laboratories are required to be registered under the select agent regulations. However, registration with DSAT is a requirement based on possession of select agents and not ownership of a BSL-4 laboratory. Therefore, if a BSL-4 laboratory, like the laboratory in Richmond, Virginia, is commissioned using simulants, and all diagnostic work is done effectively by using biochemical reagents, gene probes, and possibly inactivated agents as controls, there would be no legal requirement for registration. Thus, CDC may not know of all BSL-4 laboratories.

BSL-3 Laboratories Are Being Built in All Sectors throughout the United States

CDC officials stated that unlike the case with BSL-4 laboratories, operators might build BSL-3 laboratories and not work with select agents. For example, when building new laboratories or upgrading existing ones, many laboratory owners may build to meet BSL-3 level containment, often in anticipation of future work, even though they intend for some time to operate at the BSL-2 level with BSL-2 recommended agents. Consequently, CDC officials acknowledged that they do not know the total number of BSL-3 laboratories in the United States that are not registered to possess, use, or transfer select agents.

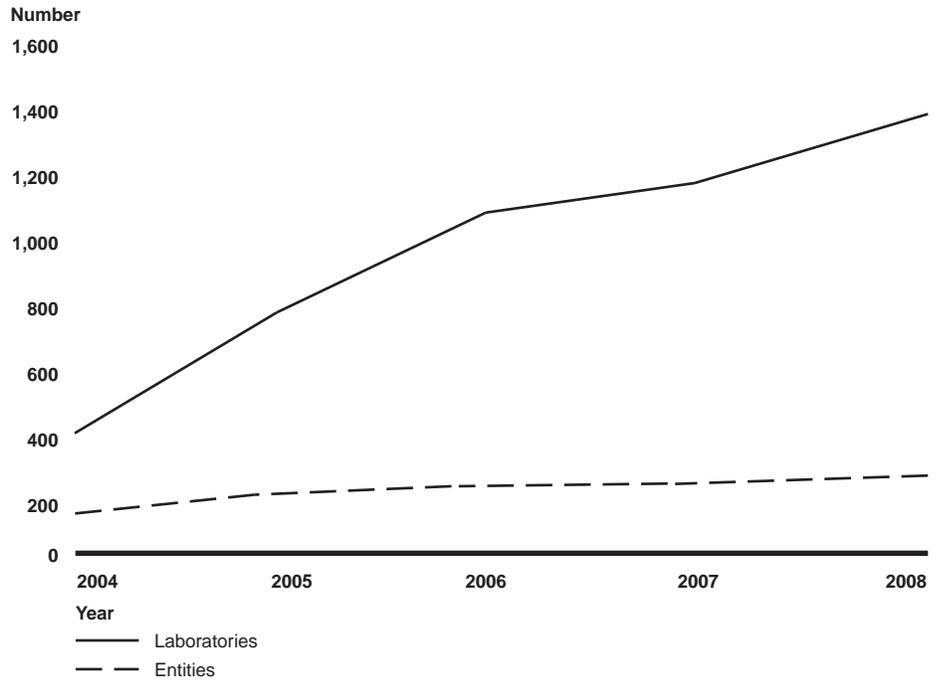
In April 2007, we conducted a Web-based survey—based on a search of publicly available sources—of contacts knowledgeable about high-containment laboratories (for example, biosafety officers).²⁷ A number of respondents who stated that their institutions had high-containment laboratories said that their laboratories were not working with select agents and were therefore not registered with the DSAT or APHIS select agent program. Although the respondents were not randomly selected, the results suggest that there may be many BSL-3 laboratories that do not work with select agents. These laboratories could potentially be tapped for use if national strategy required additional capacity.

In 2004, there were far more entities registered with CDC that maintained BSL-3 laboratories than BSL-4 laboratories (150 versus 5), and this number grew to 242 in 2008. As shown in figure 2, these entities accounted for a total of 415 registered BSL-3 laboratories in 2004; this number grew to 1,362 by 2008 (a more than three-fold increase).²⁸

²⁷The response rate for the survey was 41 percent. See appendix I for additional details.

²⁸Entities may define a laboratory as one room or a series of rooms.

Figure 2: BSL-3 Laboratories Maintained by Entities Registered with DSAT, by Calendar Year and Sector



Source: GAO analysis based on NIAID information.

Between 2004 and 2008, the largest increase occurred in the academic sector (from 120 to 474, an increase of 354 laboratories) followed by the federal government (from 130 to 395, an increase of 265 laboratories). Table 4 details these increases.

Table 4: BSL-3 Laboratories Maintained by Entities Registered with DSAT, by Calendar Year and Sector

Year	Number of entities	Number of laboratories	Sector				
			Federal government	State/local government	Academic	Private (nonprofit)	Commercial (for profit)
2004	150	415	130	118	120	28	19
2005	210	782	192	171	299	76	44
2006	237	1,086	271	220	438	95	62
2007	238	1,176	347	254	388	119	68
2008	242	1,362	395	295	474	125	73

Source: DSAT program as of February 2009.

Note: Laboratories may be defined by the entity as one room or a series of rooms (e.g., a suite).

APHIS experienced only a slight increase in the entities with BSL-3 laboratories that registered between 2004 and 2007 (from 41 to 45); however, in 2008, APHIS transferred 8 BSL-3 facilities to DSAT as the result of a change in the select agent list rules. Overall, the number of entities registered with APHIS was much lower than DSAT's total. (See table 5.)

Table 5: BSL-3 Laboratories Maintained by Entities Registered with APHIS, by Calendar Year and Sector

Year	Number of entities	Number of laboratories	Sector				
			Federal government	State/local government	Academic	Private (nonprofit)	Commercial (for profit)
2004	41	290	179	10	42	20	39
2005	42	293	179	10	48	20	36
2006	44	299	179	15	49	20	36
2007	45	303	179	15	48	20	41
2008	37 ^a	281	179	8	45	20	26

Source: APHIS, June 2009.

Note: The number of laboratories includes BSL-3 and ABSL-3 laboratories.

^aEight APHIS BSL-3 entities were transferred to CDC as a result of the select agent list rule change in 2008.

As shown in table 6, the size of the state public health laboratories network increased following the 2001 anthrax attacks. According to a survey conducted by the Association of Public Health laboratories (APHL) in August 2004, state public health laboratories have used public health preparedness funding since 2001 to build, expand, and enhance BSL-3 laboratories.²⁹ In 1998, APHL found that 12 of 38 responding states reported having a state public health laboratory at the BSL-3 level. As of March 2009, all 50 states had at least one state public health BSL-3 laboratory.³⁰

²⁹Association of Public Health Laboratories, *Public Health Laboratory Issues in Brief: Bioterrorism Capacity* (Washington D.C., April 2005).

³⁰Personal communication from APHL, March 2009.

Table 6: BSL-3 Laboratories in the State Public Health System

Calendar year	State public health BSL-3 laboratories
2001	69
2002	71
2003	139

Source: Association of Public Health laboratories, 2005.

Since the anthrax attacks of 2001, BSL-3 laboratories have started to expand geographically as well as by sector. As mentioned above, because individual states need to respond to bioterrorist threats, all 50 states now have some BSL-3 level capacity—at least for diagnostic and analytical services—to support emergency response.³¹

Additionally, NIAID recently funded the construction of 13 BSL-3 Regional Biocontainment Laboratories (RBL) within the academic research community at the following universities:

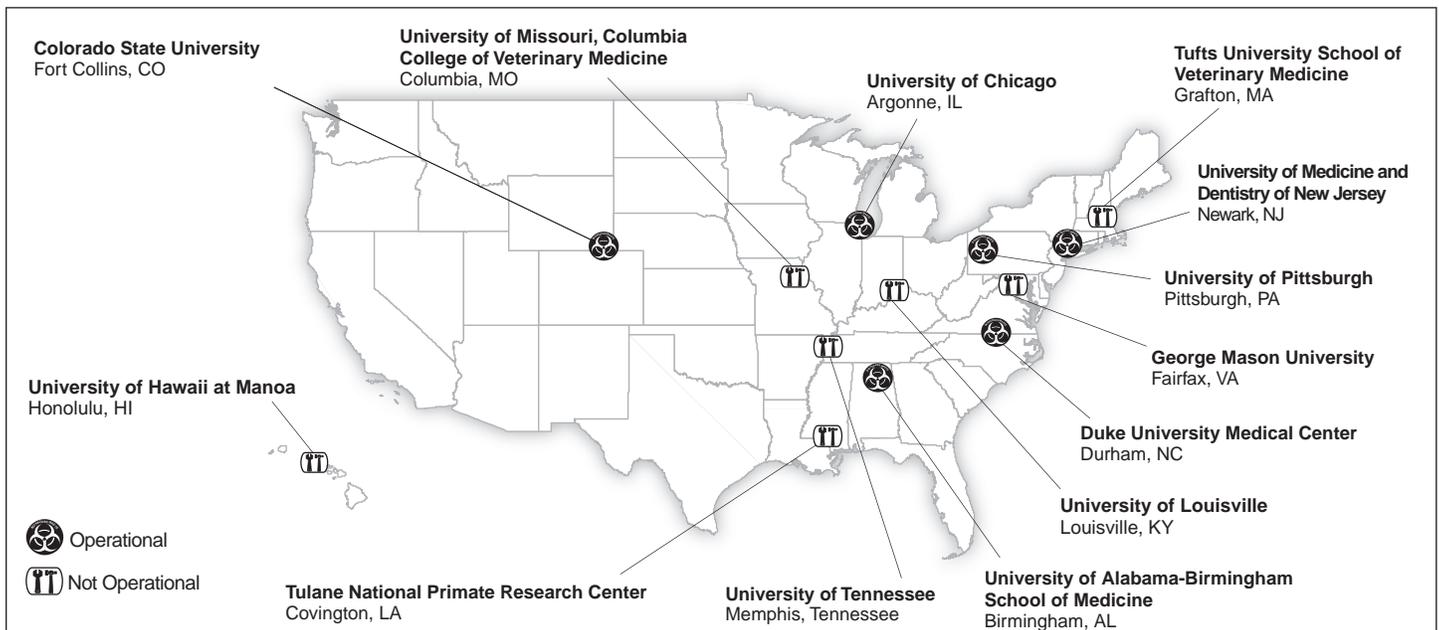
- (1) Colorado State University, Fort Collins, Colorado;
- (2) Duke University Medical Center, Durham, North Carolina;
- (3) George Mason University, Fairfax, Virginia;
- (4) University of Hawaii, Manoa, Hawaii;
- (5) University of Louisville, Louisville, Kentucky;
- (6) University of Medicine and Dentistry of New Jersey; Newark, New Jersey;
- (7) Tufts University, Grafton, Massachusetts;
- (8) Tulane National Primate Research Center, Covington, Louisiana;
- (9) University of Alabama, Birmingham, Alabama;
- (10) University of Chicago, Argonne, Illinois;
- (11) University of Missouri, Columbia, Missouri;
- (12) University of Pittsburgh, Pittsburgh, Pennsylvania; and
- (13) University of Tennessee Health Science Center, Memphis, Tennessee.

³¹We reported on the importance of building adequate laboratory capacity to respond to both natural and terrorist-related outbreaks. See *West Nile Virus Outbreak: Lessons for Public Health Preparedness* (GAO/HEHS-00-180, Sept. 11, 2000) and *Infectious Disease Outbreaks: Bioterrorism Preparedness Efforts Have Improved Public Health Response Capacity, But Gaps Remain* (GAO-03-654T, Apr. 9, 2003).

NIAID is constructing RBLs to provide regional BSL-3 laboratory capacity to support NIAID's Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Research. The RBLs are distributed regionally around the country.

Figure 3 shows the sites of NIAID-funded RBLs in the United States.

Figure 3: BSL-3 Laboratories Maintained by Entities Registered with APHIS, by Calendar Year and Sector



Source: GAO design based on NIAID information. Art Explosion (map).

The Workforce in BSL-3 and BSL-4 Laboratories Is Increasing

As expected, with an increase in the number of entities and laboratories that work with select agents, the number of individuals DSAT approved for access to work in the laboratories increased between 2004 and 2008. Table 7 shows the total number of individuals with active access approvals from DSAT and APHIS.

Table 7: Individuals with Active Access Approvals from DSAT and APHIS, by End of Calendar Year and Sector

Year	Number of individuals ^a	Sector				
		Federal government	State/local government	Academic	Private (nonprofit)	Commercial (for-profit)
2004	8,335	2,629	1,986	2,309	784	627
2005	9,603	2,776	2,280	2,760	982	805
2006	10,134	2,912	2,420	3,006	975	821
2007	10,473	3,067	2,517	3,090	1,004	795
2008	10,365	3,006	2,384	3,110	1,036	829

Source: DSAT, as of February 2009.

Note: Data from DSAT and APHIS are available only from 2004 to the present as entities were not required to be fully registered until November 12, 2003.

^aTotals include laboratory staff and laboratory support staff (e.g., maintenance, security, and IT support) with access approvals from DSAT for BSL-2, BSL-3, and BSL-4 laboratories and not the total number of staff that work with select agents.

In 2004, 8,335 individuals had access approvals. This number increased to 10,365 by 2008.³² The largest growth was in the academic sector. In 2004, 2,309 individuals in the academic sector had access approvals; this number increased to 3,110 by 2008 (an increase of 801 workers). In addition to those workers approved by DSAT, 4,149 individuals had access approvals through APHIS as of February 2009. It is important to note that as the number of new entities and high-containment laboratories increases, many new workers are being hired to work in these laboratories. However, not much is currently known about the characteristics of this workforce because there are no requirements in the select agent regulations to report on qualifications. In addition, there are no national standards for training of workers or standardized certification programs to test the proficiency of these workers.

³²DSAT officials told us that their current database includes data on (1) the number of workers approved to have access to select agents and toxins by CDC or APHIS following a security risk assessment by the FBI and (2) workers who work with select agents in BSL-2 laboratories. However, DSAT officials are now working on a system that will be able to show the number of workers by type of laboratory (for example, BSL-2, BSL-3, and BSL-4) and type of worker (for example, laboratory staff and support staff). In accordance with 42 C.F.R. 73.10, security risk assessments are conducted on all individuals who wish to gain access to select agents. Following the completion of that assessment, an individual is granted access approval to select agents provided that the individual is not identified as a restricted person as defined in section 175b of title 18 of the United States Code.

Budget and Resources for Select Agent Oversight Program

The increase in the number of entities and high-containment laboratories that work with select agents has implications for federal oversight. As part of regulatory requirements, DSAT and APHIS staff inspect each entity prior to issuing a certificate of registration to ensure that the entity is in compliance with the select agent regulations. In addition, as part of the entity’s renewal process, which occurs every 3 years, DSAT and APHIS inspectors are required to reinspect the entity. APHIS performs additional annual compliance inspections between the 3-year renewal cycles even if there is no change. DSAT performs additional inspections when an entity adds a select agent or toxin, a new laboratory facility, or a new procedure that requires verification of the entity’s biosafety plans and procedures.

As mentioned previously, the number of entities and the number of BSL-3 laboratories working with select agents increased between 2004 and 2008. As a result of this increase, DSAT now has to inspect more entities.

As shown in table 8, DSAT had a budget of \$14 million and had 25 full-time equivalent inspectors (5 federal and 20 contract) in fiscal year 2004, when the interim regulations first provided for certificates of registration. However, its budget decreased between 2004 and 2008. In 2004, DSAT was responsible for providing oversight to 150 entities with 415 BSL-3 laboratories. In 2008, DSAT provided oversight to 242 entities with 1,362 BSL-3 laboratories with a decreased budget and only 3 more inspectors (11 federal and 17 contract). No evaluations are available to determine how this increased mission and decreased budget affected the quality of oversight.

Table 8: DSAT Budget and Staff for Select Agent Oversight Program by Fiscal Year

Fiscal year	DSAT budget (current dollars in millions) ^a	Total DSAT staff		DSAT inspectors	
		Federal staff ^b	Contract staff ^c	Federal inspectors	Contract inspectors
2004	\$14.2	18	58	5	20
2005	\$13.5	17	63	6	23
2006	\$13.0	16	64	9	22
2007	\$14.3	18	60	10	17
2008	\$12.1	22	64	11	17

Source: DSAT, April 2009.

Notes:

(1) DSAT budget and staffing figures include both the select agent program and the etiological agent import permit program.

(2) As of April, 2009, the estimated fiscal year 2009 budget for DSAT was \$13.6 million. There currently are 23 federal staff (10 inspectors) and 64 contract staff (20 inspectors) assigned to DSAT.

^aThis represents the total DSAT budget (ceilings).

^bThese figures reflect the actual number of federal employees working in DSAT at the end of the fiscal year and do not include vacant positions. However, they do include the number of federal inspectors.

^cThese figures include the number of contract staff (e.g., inspectors, data entry personnel, and record managers) assigned to DSAT at the end of the fiscal year.

Before 2005, when APHIS had no select agent line item, it funded select agent program activities using a variety of existing funding sources (e.g., homeland security). As shown in table 9, APHIS received a budget of \$2.5 million in fiscal year 2005. APHIS officials estimate that the service has devoted about 5 staff years to select agent inspections for each year since 2006. No evaluations are available to determine whether APHIS has sufficient resources to carry out its mission.

Table 9: APHIS’s Budget and Staff for Select Agent Oversight Program

Fiscal year	APHIS budget (current dollars in millions ^a)	APHIS Staff			
		Federal staff ^b	Contract staff	Federal inspectors (staff years) ^c	Contract inspectors
2004	-	-	0	3	0
2005	\$2.5	6	0	4	0
2006	\$3.5	18	0	5	0
2007	\$3.5	18	0	5	0
2008	\$4.2	18	0	5	0
2009	\$5.2	22	0	5	0

Source: APHIS, May 2009.

^aThese budget numbers represent dollars allocated to APHIS for the Agricultural Select Agent Program.

^bThe number of federal staff represents not only staff members who devote 100 percent of their time to the regulatory program but also part-time commitments of support personnel, including select agent entity inspectors (see footnote c).

^cThe number of federal inspectors represents the staff years APHIS devotes to select agent inspections. APHIS inspections of select agent laboratories are performed by APHIS veterinarians/inspectors stationed throughout the United States and two select agent staff members stationed in Riverdale, Maryland. These inspectors also perform other similar duties—for example, inspections of entities and containment facilities in support of APHIS’s permitting system pursuant to the Animal Health Protection Act and the Plant Protection Act. For this reason, the number of staff years APHIS devotes to select agent inspections is less than the number of trained inspectors. APHIS estimates that it has devoted about 5 staff years annually to select agent inspections since 2006.

No Federal Agency Has the Mission to Track the Expansion of All High-Containment Laboratories and Regulate Biosafety in the United States

Currently, no executive or legislative mandate directs any federal agency to track the expansion of all high-containment laboratories. Because no federal agency has the mission to track the expansion of BSL-3 and BSL-4 laboratories in the United States, no federal agency knows how many such laboratories exist in the United States. While there is a consensus among federal agency officials and experts that some degree of risk is always associated with high-containment laboratories, no one agency is responsible for determining, or able to determine, the aggregate or cumulative risks associated with the expansion of these high-containment laboratories.³³

As shown in table 10, none of the 12 federal agencies that responded to our survey indicated that they have the mission to track and know the number of all BSL-3 and BSL-4 laboratories within the United States.

Table 10: Federal Agencies without a Mission to Track and Know the Number of All BSL-3 and BSL-4 Laboratories within the United States

Agency	Mission to track	Know the number
Department of Commerce	No	No
Department of Defense	No	No
Department of Energy	No	No
Department of Health and Human Services	No	No
Department of Homeland Security	No	No
Department of Interior	No	No
Department of Justice	No	No
Department of Labor	No	No
Department of State	No	No
Department of Veterans Affairs	No	No
Environmental Protection Agency	No	No
U.S. Department of Agriculture	No	No

Source: GAO Survey of Federal Agencies Involved with BSL-3 and BSL-4 laboratories, 2007.

While some federal agencies do have a mission to track a subset of BSL-3 and -4 laboratories that work with select agents and know the number of those laboratories, no single regulatory agency has specific responsibility for biosafety in all high-containment laboratories in the United States.

³³ Aggregate risks are defined as the sum total of all the risk elements associated with operating a high-containment laboratory.

According to some experts and federal agency officials, the oversight of these laboratories is fragmented and relies on self-policing. For example, if an entity is registered under the select agent regulations, DSAT or APHIS provides oversight. On the other hand, if an entity receives federal funding from NIH for rDNA research, the NIH Office of Biotechnology Activities provides oversight. These agencies assume that all risks would be dealt with by the entities' self-regulation, consistent with the laboratory practice guidelines developed by NIH and CDC.³⁴

Risks Associated with the Expansion of High-Containment Laboratories

Several federal agencies told us that they should know the number and location of all BSL-3 and -4 laboratories to carry out their agency missions. Some intelligence agencies, for example, indicated that—if there is another incident similar to the 2001 anthrax attacks—they would need to know the number and location of high-containment laboratories that do not work with select agents within the United States to identify all potential sources that could have been used to prepare the material. These officials told us that a determined scientist could easily take a small quantity of a select agent from his or her laboratory to a non-select-agent laboratory to grow the material.

According to these intelligence agencies, these high-containment laboratories represent a capability that can be targeted by terrorists or misused by insiders with malicious intent.³⁵ While some agencies have the specific responsibility for determining threats from rogue nations and foreign and domestic terrorists, we found that no agency has the mission to proactively determine the threat from insiders.

According to most experts, there is a baseline risk associated with any high-containment laboratory. With expansion, the aggregate risks increase. However, no agency has the mission to determine whether the risks

³⁴HHS has established a Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight to undertake an intensive analysis of the current framework of biosafety and biocontainment oversight of research activities involving infectious agents and toxins in high- and maximum-containment research facilities with the goal of exploring strategies to address concerns voiced by Congress and the general public. The task force is chaired by officials from HHS and UDSA and comprises representatives from a broad range of federal departments and agencies that have responsibility for and oversight of the management of biohazard risks.

³⁵Some intelligence agencies have a mission to track and a need to know the number of all BSL-3 and BSL-4 laboratories or their equivalents abroad. However, they do not know the total number of those laboratories.

associated with expansion increase in proportion to the number of laboratories or at some different rate or whether factors such as location and resource limitations may affect the risk ratio. Because CDC and USDA regulations require that entities registering with the select agent program assess only the risks associated with their individual laboratories, CDC and USDA do not have the mission to determine the aggregate risks associated with the expansion of high-containment laboratories that work with select agents.

High-containment laboratories can pose health risks for individual laboratory workers as well as the surrounding community. However, the relative risk profile of new versus more established laboratories is not known. According to CDC officials, the risks from accidental exposure or release can never be completely eliminated, and even laboratories within sophisticated biological research programs—including those most extensively regulated—have had and will continue to have safety failures.

In addition, while some of the most dangerous agents are regulated under the CDC-APHIS select agent program, high-containment laboratories also work with agents not covered under this program. Laboratories outside the select agent program, especially those working with emerging infectious diseases, can also pose biosafety risks from accidental exposure or release. Several of these biological agents are listed in the BMBL as requiring BSL-3 practices, including West Nile Virus and Hantavirus. (See appendix IV for a list of biological agents recommended to be handled in BSL-3 laboratories that are not select agents).

Consequently, laboratories having capabilities to work with biological agents, even though they do not possess select agents, are not currently subject to oversight. These laboratories also have associated biosecurity risks because of their potential as targets for terrorism or theft by either internal or external perpetrators. Laboratories outside the select agent program also represent a capability that can be paired with dangerous pathogens and skilled but ill-intentioned scientists to become a threat.

Unlike the United Kingdom, the United States Has No Laws to Assist in Tracking High-Containment Laboratories

Currently, no laws in the United States specifically focus on all high-containment laboratories. In the United Kingdom (U.K.), by contrast, new high-containment laboratories that work with human, animal, or genetically modified (GM) pathogens need to notify the U.K. regulator (the Health and Safety Executive (HSE)) and receive either consent (for GM human pathogens) or license (for animal pathogens) before they commence their activities.

Prior to construction of the facility, there is no requirement to inform HSE (except for planning authorities, who look at land use and building quality); however, in practice, HSE staff are involved at the design stage and at various points during the construction process. According to HSE staff, this early involvement has been extremely helpful in ensuring that new facilities meet the standards set out in the legislation and supporting guidance (related to the management, design, and operation of high-containment laboratories).

This involvement has also enabled HSE to address the application of new technologies in high-containment laboratories (e.g., alkaline hydrolysis for waste destruction as an alternative to incineration). While the legislation in the U.K. states that a BSL-4 laboratory must have an incinerator on site for disposal of animal carcasses, HSE staff told us that they have been involved in discussions relating to new facilities where the entities wanted to replace the incinerator with an alkaline hydrolysis system. Similarly, all BSL-4 laboratories use cabinet lines (for human pathogens). HSE staff have been in discussion with entities about proposals to move to a suited system rather than rely entirely on primary containment. HSE staff told us that they are recognizing that technologies change and there may be good reasons to move away from established procedures, assuming that the alternatives being proposed provide a high degree of assurance that biosafety and biosecurity will not be compromised by the changes.

In April 2010, the U.K. plans to implement a single regulatory framework for human, animal, and genetically modified pathogens that will include a legal requirement for duty holders to consult the regulatory authority prior to construction and for HSE to be a statutory consultee as part of the planning authorization.³⁶

³⁶The current legislation that authorizes work with these high hazard pathogens is Control of Substances Hazardous to Health (COSHH) Regulations 2002, Genetically Modified Organisms (Contained Use) Regulations 2000 (as amended 2005), and Specified Animal Pathogens Order 2008.

Lessons Learned from Four Incidents Highlight the Risks Inherent in the Expansion of High-Containment Laboratories

We reviewed four incidents that highlight the risks inherent in the expansion of high-containment laboratories: alleged insider misuse of a select agent and laboratory; Texas A&M University's (TAMU) failure to report to CDC exposures to select agents in 2006; power outages at CDC's high-containment laboratories in 2007 and 2008; and the release of foot-and-mouth disease virus in 2007 at the Pirbright facility in the U.K.

We reviewed these incidents in detail because they represented different types of risk associated with high-containment laboratories and because a significant amount of information was available concerning them. According to the experts we talked with, many other incidents and accidents have occurred, mainly as a result of human error or equipment failure. Fortunately, most incidents/accidents do not have serious consequences for the health of laboratory workers, the general population, or the environment. The experts we spoke with also stated that it is highly probable that many incidents go unreported and unrecorded because of the lack of such serious consequences. Such underreporting represents lost opportunities to analyze and learn lessons that can provide a basis for continuing improvement and maintenance of laboratory safety.

We are not making any generalizations about the magnitude of the problem involving other laboratories. However, the lessons we have identified highlight ways to improve biosafety and biosecurity. These lessons also have implications for institutional and federal oversight.

Incident 1: Alleged Insider Misuse of a Select Agent and Laboratory

In September and October 2001, letters containing spores of *B. anthracis* powder were distributed through the U.S. postal system to two senators, Thomas Daschle and Patrick Leahy, and members of the media.³⁷ The

³⁷The anthrax attacks came in two waves. The first set of anthrax letters had a Trenton, New Jersey, postmark dated September 18, 2001, exactly 1 week after the September 11, 2001, attacks. Three letters are believed to have been mailed at this time to NBC News and the *New York Post*, both located in New York City, and to the *National Enquirer* at American Media, Inc., in Boca Raton, Florida. Two more anthrax letters, bearing the same Trenton postmark, were dated October 9, 3 weeks after the first mailing. The letters were addressed to two Democratic Senators, Thomas Daschle of South Dakota and Patrick Leahy of Vermont.

letters led to the first U.S. cases of anthrax disease related to bioterrorism, and the subsequent investigation by FBI has been called “Amerithrax.”³⁸

On August 6, 2008, the FBI alleged that the “sole culprit” in the 2001 anthrax attacks was Dr. Bruce Ivins, a U.S. Army scientist with a Ph.D. in microbiology who had worked for 28 years at the U.S. Army Medical Research Institute for Infectious Diseases (USAMRIID) at Ft. Detrick, Maryland.³⁹ USAMRIID is the only DOD laboratory with the capability to study highly dangerous pathogens requiring maximum containment at BSL-4. Dr. Ivins had helped develop an anthrax vaccine for U.S. troops and was in charge of producing large quantities of wet anthrax spores for research.

Immediately following the anthrax mailings in 2001, FBI took contaminated evidence to USAMRIID for analysis. Dr. Ivins was tasked by USAMRIID management to analyze the samples of spores sent through the mail and was also a technical consultant to the FBI in the early months of investigation. In March 2003, Dr. Ivins and two of his colleagues at USAMRIID received the Decoration for Exceptional Civilian Service—the highest award given to DOD civilian employees—for helping solve technical problems in the manufacturing of licensed anthrax vaccine.

In December 2001, one of Dr. Ivins’ coworkers told Dr. Ivins that she observed on several occasions unsafe handling procedures by Diagnostic System Division personnel. She also told him that she might have been exposed to anthrax spores when handling an anthrax-contaminated letter. Dr. Ivins began sampling areas in the laboratory space that might have been contaminated with anthrax. He took samples from the shared office areas and later decontaminated her desk, computer, keypad, and monitor. However, he neither documented this incident in the Army record log

³⁸The postal facilities in New Jersey and Washington, D.C., that processed the senators’ letters became heavily contaminated. Other mail routed through these and other postal facilities also became contaminated. Numerous federal facilities in the Washington, D.C., area—the U.S. Supreme Court and main State Department buildings—were also found to be contaminated. The mail for these federal facilities was believed to have either come in direct contact with the contaminated letters or passed through sorting equipment at the postal facility that processed the letters. In all, 22 individuals contracted anthrax disease in four states (Connecticut, Florida, New Jersey, and New York) and Washington, D.C. Five of the 22 individuals died.

³⁹USAMRIID is an Army installation with BSL-3 and BSL-4 laboratories. These laboratories work with select agents and toxins. USAMRIID is regulated by DOD because it is a military laboratory and by CDC because it works with select agents and toxins.

book nor notified his superiors. He later acknowledged to Army officials that this was a violation of protocol. Dr. Ivins' behavior was detailed in an Army investigation⁴⁰ conducted in response to a second round of sampling he conducted in April, but his name did not surface at that time as a suspect in the anthrax attacks.

After a spill incident inside of suite B-3 in building 1425 in April 2002, Dr. Ivins conducted a second round of unauthorized sampling of his shared office space and cold side areas outside of suite B-3. These findings were reported and sparked a buildingwide sampling inspection. An inspection conducted by the Army 7 months after the anthrax mailing found that suite B-3 in building 1425 at USAMRIID was contaminated with anthrax in four rooms of suite B-3 (306, 304, cold room, and 313 (Dr. Ivins's laboratory)) and that the bacteria had escaped from secure to unprotected areas in the building. All the areas outside of suite B-3 that tested positive were associated with Dr. Ivins and members of the Bacteriology Division. The inspection report stated that "safety procedures at the facility and in individual laboratories were lax and inadequately documented; that safety supervision sometimes was carried out by junior personnel with inadequate training; and that exposures of dangerous bacteria at the laboratory, including anthrax, had not been adequately reported." (See appendix V for additional information on the U.S. Army's requirements for high-containment laboratories at the time of the 2001 anthrax incidents.)

In 2005, the FBI investigation began to shift to a particular laboratory at USAMRIID, and it began to focus on Dr. Ivins as a suspect in 2007. According to the FBI, Dr. Ivins had the necessary expertise and equipment to make the anthrax powder in his laboratory. Specifically, at the time of the anthrax mailings, Dr. Ivins possessed extensive knowledge of various anthrax production protocols. He was adept at manipulating anthrax production and purification variables to maximize sporulation and improve the quality of anthrax spore preparations. He also understood anthrax aerosolization dosage rates and the importance of purity, consistency, and spore particle size due to his responsibility for providing liquid anthrax spore preparations for animal aerosol challenges. He also had used lyophilizers, biological safety cabinets, incubators, and centrifuges in vaccine research. Such devices are considered essential for

⁴⁰Department of the Army, "AR 15-6 Investigation Into Anthrax Contamination at USAMRIID," May 16, 2002.

the production of the highly purified, powdered anthrax spores used in the fall 2001 mailings.

According to the FBI's application for a search warrant, at the time of the attack, Dr. Ivins "(1) was the custodian of a large flask of highly purified anthrax spores that possess certain genetic mutations identical to the anthrax used in the attacks; (2) Ivins has been unable to give investigators an adequate explanation for his late night laboratory work hours around the time of both anthrax mailings; (3) Ivins has claimed that he was suffering serious mental health issues in the months preceding the attacks, and told a coworker that he had 'incredible paranoid, delusional thoughts at times' and feared that he might not be able to control his behavior; (4) Ivins is believed to have submitted false samples of anthrax from his laboratory to the FBI for forensic analysis in order to mislead investigators; (5) at the time of the attacks, Ivins was under pressure at work to assist a private company that had lost its FDA approval to produce an anthrax vaccine the Army needed for U.S. troops, and which Ivins believed was essential for the anthrax program at USAMRIID; and (6) Ivins sent an e-mail to a friend a few days before the anthrax attacks warning her that 'Bin Laden terrorists for sure have anthrax and sarin gas' and have 'just decreed death to all Jews and all Americans,' language similar to the anthrax letters warning 'WE HAVE THIS ANTHRAX ... DEATH TO AMERICA ... DEATH TO ISRAEL.'"⁴¹ The FBI stated that in late 2005, forensic science (genetic analysis) used to trace the anthrax used in the 2001 attack had genetic markers consistent with the anthrax spores kept in a flask in the refrigerator in Dr. Ivins's laboratory at Ft. Detrick, Maryland, to spores in the letters.

During this time, Dr. Ivins kept his security clearance and passed a polygraph-assisted interrogation (also known as a "lie detector test") in which he was questioned about his possible participation in the anthrax attacks. In November 2007, he was denied access to all high-containment laboratories and, in March 2008, to all laboratories at USAMRIID. It should be noted that while Dr. Ivins was denied access to the high-containment suites in November 2007, he was certified at that time into the personnel reliability program. On July 10, 2008, Dr. Ivins attended a briefing on a new pneumonic plague vaccine under development at the Army's laboratory. After this briefing, he was escorted to a psychiatric evaluation off the

⁴¹Application and Affidavit for Search Warrant Case Number 08-432, available at www.fbi.gov/page2/amerithrax-affidavits/07-524-M-01.pdf. (accessed on June 29, 2009)

installation by local authorities, and his access rights to the entirety of USAMRIID were withdrawn by the laboratory commander. An order was subsequently issued to installation security to prevent Dr. Ivins from entering the installation unescorted. A written bar order was signed with a plan to serve the document to Dr. Ivins. Before service of the order occurred, he died of a drug overdose on July 29, 2008.

Lessons Learned: Insider Risk and Inventory Control of Biological Agents

This incident highlights two lessons: (1) an ill-intentioned insider can pose a risk not only by passing on confidential information but also by removing dangerous material from a high-containment laboratory, and (2) it is impossible to have completely effective inventory control of biological material with currently available technologies. It is impossible to know the exact number of bacteria or virus in a laboratory's inventory or working stocks at any specific time. At Ft. Detrick, ineffective procedures for the control of inventories and the unlimited use of laboratory facilities allegedly allowed Dr. Ivins the opportunity to pursue his own ends. As the number of high-containment laboratories increases, there will be an increase in the pool of scientists with expertise and, thus, the corresponding risk from insiders may also increase.

Insiders Can Misuse Material and Facilities

There are arguably two aspects to insider risk: the motive of the insider and the ability to misuse material and laboratory facilities. These two elements need to be understood if effective countermeasures are to be instituted in a proportionate manner. In this case, assuming Dr. Ivins was the culprit, no one can conclusively determine what motivated his actions since he committed suicide before his motive could be determined.

With regard to the ability to misuse the facility, FBI records show that Dr. Ivins had unlimited access to material and laboratory facilities. However, it is still unclear whether the spores in the letters came directly from the flask under Dr. Ivins's control or involved some further illicit culturing. In either case, material was illegally removed and laboratory facilities were misused—at a minimum, to dry and process the spores. It follows that research laboratories clearly represent a significant capability that can be potentially misused, and this capability is growing with the increasing number of high-containment laboratories. While efforts to strengthen inventory controls, assess and monitor personnel, and prevent facility misuse (for example, by video monitoring) have been undertaken to

address insider threats, we are not aware of any evaluation of the effectiveness of these measures.⁴² While there are clearly major difficulties in imposing such controls in research laboratories, insider risk needs to be recognized and evaluated.⁴³

Assuming that Dr. Ivins was the perpetrator in the anthrax attacks, he represents one rogue insider in a period of some 60 years, during which several thousand scientists and technicians had the opportunity to commit similar crimes. Thus, the probability of repeating that one event is, historically, very small. Devising any program to reliably reduce that figure for biological laboratory personnel is challenging. Furthermore, some DOD biological laboratory scientists and academicians we spoke with have pointed out that highly intrusive personnel reliability programs, which rely on profiling to identify insider threats, can have a negative effect on staff morale and performance by institutionalizing the concept that no one can be trusted.⁴⁴

The National Science Advisory Board for Biosecurity reported that there is little evidence that personnel reliability measures are effective or have predictive value in identifying individuals who may pose an insider threat.⁴⁵ In its report, the board recommended that “it is appropriate to enhance personnel reliability measures for individuals with access to select agents, but promulgation of a formal, national personnel reliability program is unnecessary at this time.”

On February 11, 2004, DOD issued a directive (5210.88), “Safeguarding Biological Select Agents and Toxins” (BSAT). This directive established security policies and assigned responsibilities for safeguarding select

⁴²While video monitoring addresses the threat of facility misuse to a certain extent, expert review of the images would be essential to determine if misuse is occurring.

⁴³In 2003, we reported on the risks an insider can pose in a high-containment laboratory working with animal diseases. See GAO, *Combating Bioterrorism: Actions Needed to Improve Security at Plum Island Animal Disease Center*, GAO-03-847 (Washington, D.C.: Sept. 19, 2003).

⁴⁴Moreover, in reaction to the September 11, 2001, terrorist attack and the subsequent anthrax incidents, Congress passed several laws (for example, the USA PATRIOT Act and the Bioterrorism Preparedness and Response Act of 2002) to combat terrorism and, in doing so, significantly strengthened the oversight of select agents and increased safeguards and security requirements.

⁴⁵Report of the National Science Advisory Board for Biosecurity, *Enhancing Personnel Reliability among Individuals with Access to Select Agents* (Washington, D.C.: May 2009).

agents and toxins. Specifically, this directive established, among other things, the following DOD policy:

“Individuals who have a legitimate need to handle or use biological select agents and toxins, or whose duties afford access to storage and work areas, storage containers and equipment containing biological select agents or toxins shall be screened initially for suitability and reliability. This means that they shall be emotionally and mentally stable, trustworthy, and adequately trained to perform the assigned duties and shall be the subject of a current and favorably adjudicated National Agency Check with Local Agency Checks and Credit Checks for military and contractor employees and an Access National Agency Check with credit checks and written inquiries for civilian employees with a reinvestigation every 5 years and they shall be evaluated on a continuing basis using the criteria issued by the [Under Secretary of Defense for Intelligence.]”

On April 18, 2006, DOD issued Instruction 5210.89, “Minimum Security Standards for Safeguarding Select Agents and Toxins.” This instruction established, among other things, the criteria and requirements for personnel regarding a biological personnel reliability program (BPRP). The purpose of a BPRP is to (1) ensure that each individual, who has authorized access to BSAT and/or supervises personnel with access to biological restricted areas and BSAT, including responsible and certifying officials, meets the highest standards of integrity, trust, and personal reliability and (2) identify any potential risk to public health, safety, and national security.

Following the announcement of the FBI anthrax investigation at USAMRIID, the Secretary of the Army organized a task force on August 7, 2008, to evaluate the U.S. Army biological surety program, including safety, security, and personnel reliability. In response, the Inter-Service Council for Biosecurity and Biosafety, General Officer Steering Committee, issued a report on December 12, 2008. This report focused on seven areas: transportation of select agents and toxins; biological safety; biological security/physical security; inspection; personnel reliability program/foreign personnel; inventory/accountability of select agents and toxins; and training of personnel. Review of all seven areas indicated that armed service policies, regulations, standards, and procedures in effect before 2008 met or exceeded all federal and DOD requirements. The services, however, agreed on the need to establish common standards in each area. In addition, on March 10, 2008, the Interagency Security Committee Standard defined the criteria and process to be used in

determining the facility security level of a federal facility as the basis for implementing governmentwide facility security standards.

In October 2008, the office of the Under Secretary of Defense for Acquisition, Technology, and Logistics asked the Defense Science Board Task Force on DOD Biological Safety and Security⁴⁶ to address the following questions:

- Are current and proposed policies in DOD and military department biological safety, security, and biological personnel reliability programs adequate to safeguard against accidental or intentional loss/misuse of biological select agents and toxins (BSAT) by external or internal actors?
- Are current DOD-related laboratories and operations that use or store BSAT meeting stringent standards for safety, security, and personnel reliability?
- How do DOD and military department programs compare with other government agency, academic, and industry programs?
- How can DOD usefully employ experience in other areas requiring the utmost safety and reliability when handling dangerous material (for example, the nuclear personnel reliability programs) for biosecurity policy development and implementation?

In May 2009, the Defense Science Board published its report. With regard to insider risk, the report concluded that “a determined adversary cannot be prevented from obtaining very dangerous biological materials intended for nefarious purposes, if not from DOD laboratories, then from other sources. The best we can do is to make it more difficult. We need to recognize this reality and be prepared to mitigate the effects of a biological attack.”⁴⁷

In October 2008, the White House Office of Science and Technology Policy asked the National Science Advisory Board for Biosecurity (NSABB) to recommend strategies for enhancing personnel reliability among

⁴⁶Memorandum for Chairman, Defense Science Board, “Defense Science Board Task Force on the Department of Defense Biological Safety and Security Program,” (Washington, D.C., October 3, 2008), p.39.

⁴⁷DOD, Report of the Defense Science Board Task Force, *Department of Defense Biological Safety and Security Program* (Washington, D.C., May 2009), p. 39.

individuals with access to biological select agents and toxins. Specifically, the NSABB was asked to identify the optimal framework for ensuring personnel reliability so that the need for biosecurity was balanced with rapid progress in the life sciences. The NSABB concluded in its report that “there is currently insufficient evidence of the effectiveness of personnel reliability program measures towards mitigating the risk of an insider threat to warrant the additional significant burden on research institutions.”⁴⁸ However, the NSABB did recommend a number of ways to enhance the culture of research responsibility and accountability at institutions that conduct select agent research, noting that the recommended actions could be accomplished without significant expenditures, resources, or disruptions of research.

On January 9, 2009, an executive order established a governmentwide working group to strengthen laboratory biosecurity in the United States.⁴⁹ The executive order asked the working group to submit to the President, no later than 180 days after the date of the order, an unclassified report, with a classified annex as required, that sets forth the following:

- “a summary of existing laws, regulations, guidance, and practices with respect to security and personnel assurance reviewed under subsection (a) of this section and their efficiency and effectiveness;
- recommendations for any new legislation, regulations, guidance, or practices for security and personnel assurance for all federal and nonfederal facilities;
- options for establishing oversight mechanisms to ensure a baseline standard is consistently applied for all physical, facility, and personnel security and assurance laws, regulations, and guidance at all federal and nonfederal facilities; and
- a comparison of the range of existing personnel security and assurance programs for access to biological select agents and toxins to personnel security and assurance programs in other fields and industries.”

⁴⁸Report of the National Science Advisory Board for Biosecurity, *Enhancing Personnel Reliability among Individuals with Access to Select Agents*, May 2009, http://oba.od.nih.gov/biosecurity/nsabb_past_meetings.html (accessed August 5, 2009).

⁴⁹Executive Order 13486, January 9, 2009, “Strengthening Laboratory Biosecurity in the United States.”

The working group submitted its draft report and recommendations to the White House on July 9, 2009. According to HHS, the draft report is to be formally reviewed and accepted by the co-chairs—the Secretaries of Defense and Health and Human Services—before it is made public.

While it may be possible to quantify the financial costs required to initiate and maintain enhanced oversight procedures—such as controls of inventories and laboratory usage—the impact of such procedures on work output is unquantifiable but nevertheless very real. According to some experts and high-containment laboratory scientists, intrusive personnel reliability programs can also have an adverse impact on staff work effectiveness.

Accordingly, the security benefits achieved by such procedures must be evaluated to obtain some understanding of the cost/benefit ratio. Such an evaluation could incorporate various stress tests and assessments of procedures against a range of risk scenarios. Effective evaluation could improve the cost/benefit ratio by concentrating on procedures with higher returns on investment and could be more acceptable to laboratory personnel by demonstrating objective benefits. Regular reevaluation is critical to avoid adding oversight procedures on a subjective rather than objective basis.

Inventory Procedures Did Not Impede Insider Misuse of Agents

Prior to the fall of 2001, there were no effective inventory control procedures at USAMRIID—or indeed other institutions that worked with select agents—that would have impeded insider misuse of such agents. Anthrax spores were held in a liquid solution in a flask (RMR-1029) that originally (October 22, 1997) contained 1000 ml of spore suspension with a concentration of 3×10^{10} spores/ml. While the flask had been under the control of Dr. Ivins since 1997, other laboratory staff may also have had access to it. However, no one in USAMRIID was specifically responsible for monitoring the use of materials by scientists. According to USAMRIID officials, Dr. Ivins's laboratory notebook contained a record of the amounts of material removed at various times between 1997 and 2004, when the FBI finally removed the flask from USAMRIID. Additional undocumented removals from the flask could have been disguised simply by adding water to restore the volume. This would have reduced the spore concentration, but this concentration was apparently never checked. Even if it had been, experts told us that the normal biological experimental error involved in counting spores could have disguised the loss of up to 5 percent of the material.

It is unclear whether the anthrax spores put in the letters came directly from the flask after being dried or whether a very small and undetectable quantity from the flask was cultured to produce enough new spores for the letters. In either scenario, the self-replicating nature of microorganisms and the inherent error associated with determining the absolute number of microorganisms in solution make inventory control a formidable if not impossible task with currently available technologies.⁵⁰

Actions Taken by the
Regulatory Agency—DSAT—
Subsequent to the Incident

According to DSAT officials, even though Dr. Ivins' alleged crime occurred prior to the expansion of the select agent regulations in 2002, DSAT performed an extensive 2-week inspection of the entire USAMRIID facility in September 2008. DSAT believes that its findings regarding USAMRIID's inventory records contributed to the decision of DOD to stand down USAMRIID operations pending a thorough review of its inventories. In addition, DSAT referred USAMRIID to the HHS-OIG for further investigation regarding the entity's apparent noncompliance with the select agent regulations. According to HHS-OIG, this referral is still an ongoing investigation.

Incident 2: Safety
Violations by a University

In 2006, a series of incidents at the high-containment laboratories at Texas A&M University (TAMU), and their aftermath, raised issues related to

- barriers to reporting laboratory accidents,
- inadequate and ineffective training for laboratory personnel,
- the failure to inform medical personnel about the agents the laboratory staff work with, and
- uncertainty about what constitutes a potential exposure.

Barriers to Reporting
Laboratory Accidents

TAMU is registered with DSAT and approved for work on several select agents. TAMU has several BSL-3 laboratories and works extensively on animal diseases, including those caused by the select agents *Brucella melitensis*, *Brucella abortus*, and *Brucella suis*. *Brucella* can cause

⁵⁰Microorganism populations are constantly in a state of flux where fractions of the total may be multiplying or dying off. This dynamic situation, coupled with the extraordinarily high numbers of organisms (billions per milliliter) and the inherent inaccuracies of assay methods, make it unrealistic to assign conclusive numbers to microbial populations in storage and working stocks.

brucellosis in humans, a disease causing flu-like symptoms, such as fever and fatigue. In severe cases, it can cause infections of the central nervous system. TAMU is also registered for use of *Coxiella burnetii*, an animal agent that can cause Q fever in humans.

In February 2006, a laboratory worker from a non-select-agent laboratory was helping out with an experiment to aerosolize *Brucella*. The laboratory worker had no familiarity with the specifics of working with *Brucella* but did have experience working with the aerosol chamber. It was later determined that the laboratory worker had been exposed to the agent while cleaning the chamber after the experiment was run.

At the time of the exposure, neither the exposed worker nor anyone else had any indication that an exposure had taken place. In fact, DSAT inspectors were on campus days after the *Brucella* exposure for a routine inspection but uncovered nothing that alerted them to what had happened.⁵¹ Symptoms did not start to appear in the exposed worker until more than a month after the exposure, and then the symptoms were flu-like. Confirmation of brucellosis was not made until another month had passed and the symptoms had worsened. However, once the brucellosis was identified, the worker notified appropriate authorities at TAMU. But no report was subsequently made to DSAT (as required by federal regulation), and a year passed before—by chance—an independent watchdog group reviewing unrelated documentation⁵² acquired through Texas’s freedom of information law, uncovered the lapse in reporting. This prompted TAMU to notify DSAT.

Training of Laboratory Personnel

The laboratory worker at TAMU who was exposed to *Brucella* was not authorized to work with that agent. The laboratory worker was, we were told, being allowed in the laboratory only to help out with operating the aerosolization chamber.⁵³ According to DSAT, TAMU failed to report to DSAT that it was conducting aerosolization work with *Brucella*. Therefore,

⁵¹The CDC inspected laboratories at TAMU on February 22, 2006, and documented 47 facility “departures” but did not note any of the violations later uncovered.

⁵²The Sunshine Project, *Mandate for Failure, The State of Institutional Biosafety Committees in an Age of Biological Weapons Research* (Austin, Texas, Oct. 4, 2004).

⁵³According to the CDC, even though the worker was escorted, having her help out with the aerosolization chamber during the *Brucella* experiments constituted unauthorized access to a select agent (since she was not authorized to work with *Brucella*) and violated regulations.

DSAT had no reason to verify training, experimental plans, and risk assessments during its inspections.

According to select agent regulations, all staff—not only staff that have access to select agents or toxins, but also staff that will work in or visit areas where select agents are handled or stored—are required to be trained in the specifics of any agent before they work with it. The training must address the particular needs of the individual, the work they will do, and the risks posed by the select agents and toxins. However, the worker at TAMU did not receive training in the specifics of *Brucella*, including its characteristics, safe handling procedures, and potential health effects.⁵⁴ While the worker was experienced in general BSL-3 procedures, her normal work regimen involved working with *Mycobacterium tuberculosis*, and her supervisor surmised that the differential in the potential for infection from *Brucella* was partially to blame for the exposure.⁵⁵ However, experts have told us that if procedures that are effective to avoid exposure to live, virulent *M. tuberculosis* were being followed correctly, these should have been effective for *Brucella* despite the differences in the infectious dose (ID₅₀).⁵⁶

The exposed laboratory worker was highly experienced in handling *M. tuberculosis*, an infectious agent. The worker had been a laboratory director of a BSL-2 laboratory for the past 5 years, had a Ph.D. in microbiology, and was by many accounts highly competent and reliable. The worker applied the procedures governing safe work with *M. tuberculosis* to the *Brucella* experiment, but her experience with *M. tuberculosis* might have provided a false sense of security.

Medical Provider Lacked Information to Diagnose Possible Infection Quickly

At the time of the exposure to *Brucella* at TAMU on February 9, 2006, the laboratory worker and others in the laboratory did not realize she had been infected. In fact, DSAT conducted a routine inspection of TAMU on February 22, 2006—13 days after the exposure—but had no way of knowing that it had happened. According to the exposed worker, she first

⁵⁴Although TAMU did not notify DSAT that it was conducting aerosolization work with *Brucella*, TAMU still had the responsibility to train the staff.

⁵⁵Although a person typically has to breathe in *M. tuberculosis* bacteria to get an infection, *Brucella* can enter the system through mucous membranes, such as those in the eyes. During the experiment, the lab worker who was exposed had been wearing a respirator that filtered the air she breathed, as is recommended for work with *M. tuberculosis*.

⁵⁶ID₅₀ is the dose needed to infect 50 percent of exposed individuals.

fell ill more than 6 weeks after the exposure. At that time, the first consultation with her physician indicated that she had the flu. Institutions generally do not give medical providers information about the specific agents that laboratory staff work with. Therefore, the physician was not alerted to the possibility that the worker's symptoms could be the result of exposure to an infectious agent. After the symptoms persisted, a consultation with an infectious disease specialist confirmed that the laboratory worker's blood contained an unknown microorganism. At that point, the worker recalled her work with *Brucella* weeks earlier. The Texas State Public Health Laboratory confirmed the infection with *Brucella* on April 16, 2006—62 days after the exposure. During the interim, the worker had resumed her normal activities.

By the time the diagnosis was made, the exposed laboratory worker had become seriously ill. The delay in recognizing the infection resulted in delay of appropriate treatment, thus aggravating her condition. Such a misdiagnosis is not uncommon with infectious diseases, as the initial symptoms often appear flu-like, and brucellosis is not generally endemic in the population. According to DSAT, the worker might have developed an even more severe infection, possibly affecting her central nervous system or the lining of her heart, if the worker had not recalled the experiment with *Brucella* and alerted her physician to this fact. The physician might have been able to correctly diagnose the infection more quickly if the physician had been informed of the agent the individual worked with.

In this incident, it was fortunate that transmission of brucellosis beyond the initial exposed individual was difficult and that there was no risk of the infection spreading to the surrounding community. Many other agents—including those that are not select agents (such as SARS coronavirus and *M. tuberculosis*)—cause diseases that are transmitted from human to human through coughing or fluid transfer.⁵⁷

Confusion over the Definition of Exposure

In addition to the incident of exposure to *Brucella*, DSAT noted that TAMU failed to report several incidents of potential exposure to *Coxiella burnetii*—a select agent and the causative agent for Q fever in humans. While the *Brucella* exposure eventually became apparent because of clinical symptoms in the laboratory worker, the *C. burnetii* incidents

⁵⁷On July 13, 2009, DSAT published a notice in the *Federal Register* proposing the addition of SARS-associated coronavirus (SARS-CoV) to the list of select agents. The *Federal Register* notice can be found at <http://edocket.access.gpo.gov/2009/pdf/E9-16536.pdf>

raised questions about what constitutes sufficient evidence of an exposure that the entity is required to report to DSAT.

For *C. burnetii* and other agents, periodically measuring the titer or antibody levels within the blood serum of laboratory workers working with those agents provides one indication of exposure. If a person's titer level is higher than his or her baseline level, then it may be concluded that the person has been exposed to the agent. In response to the draft report, HHS stated that the titer should be at least four times higher than baseline to be considered an exposure. However, HHS did not provide any support for its assertion, and we could not find any scientific support for picking this level.

We consider that any titer elevation where that agent is being worked with in the laboratory requires further detailed investigation. In addition, the degree of titer elevation that can be considered as definitively diagnostic needs to be scientifically validated on an agent-by-agent basis. However, there are issues with using titer levels as an indication of exposure. For example, determining when the exposure took place is not straightforward, and methods for determining titers are not standardized across laboratories.

TAMU has a program to monitor blood serum for those staff working with *C. burnetii*. While humans are very susceptible to Q fever, only about one-half of all people infected with *C. burnetii* show signs of clinical illness. During the DSAT inspection that was triggered by the uncovering of the *Brucella* incident, DSAT came across clinical records showing that several laboratory workers had elevated titers for *C. burnetii*. No reports of this possible exposure had been sent to DSAT. DSAT noted this issue and, on April 24, 2007, TAMU submitted the required Form 3 to DSAT.

However, as a result of subsequent discussion with the individuals who had the elevated titers, TAMU officials began to doubt whether the elevated titers resulted from exposures that had occurred at TAMU. In one case, TAMU said, one of the infected laboratory workers had only recently been hired by TAMU but had worked in a clinical laboratory in China where *C. burnetii* was known to have been present. It is not clear how the elevated titer related to the employee's baseline titer taken at the time of employment. In another case, the worker claimed to have been exposed many years earlier and to have always registered high, although the actual levels varied. DSAT officials disagreed with this interpretation and believed the high titers resulted from exposures at TAMU.

TAMU officials told us that they initially responded to the uncovering of the elevated titer incidents by reporting to DSAT any subsequent elevated titer level identified in its laboratory workers. TAMU also told us that it is now unsure how to proceed; it has notified DSAT that, in its opinion, an exposure suggested by an elevated titer should be defined as having occurred only after clinical symptoms appear in the individual. TAMU has, therefore, ceased reporting incidents where there are only elevated titers. In the absence of clarity over the definition of exposure, TAMU officials have chosen to define it as they see fit.

DSAT officials told us that they disagreed with TAMU's interpretation. Reporting exposures only after clinical symptoms develop could have dangerous consequences for laboratory workers and even the public. DSAT conducted multiple follow-up inspections to assist TAMU in becoming compliant with the select agent regulations. In addition, on January 18, 2008, DSAT and APHIS posted a guidance document on the analysis of possible exposure incidents.⁵⁸ According to DSAT, scenario 20 of this document specifically addresses the recommended response to an elevated antibody titer in a select agent worker. DSAT officials noted that reporting exposures only after clinical symptoms develop—given the requirements of the select agent regulations and the guidance provided in the theft, loss, and release guidance document—would be considered a violation of the select agent regulations.

Lessons Learned: Barriers to Reporting, Compliance with Regulations Regarding Training, Informing Medical Providers, and Defining Exposure

The common theme in the TAMU incidents was a lack of rigor in applying fundamental safety and training procedures coupled with a culture that embodied a reluctance to be open about problems both within the organization and with the regulator. According to our experts, such cultural reticence has historically been a factor in many previous incidents and can be remedied only by appropriate leadership at the highest level of the organization coupled with robust and continued action by the regulator.

Barriers to Reporting Need to Be Identified and Overcome

According to the literature and discussions with federal officials and experts, accidents in laboratories do occur, mostly as a result of human error due to carelessness, inadequate training, poor judgment, fatigue, or a

⁵⁸See www.selectagents.gov/resources/CDC-APHIS_Theft_loss_Release_Information_Document.pdf.

combination thereof.⁵⁹ In the case of theft, loss, occupational exposure, or release of a select agent, the laboratory must immediately report certain information to DSAT or APHIS.

It has been suggested that there is a disincentive to report laboratory-acquired infections and other mishaps at research institutions because it could result in (1) negative publicity for the institution and the worker or (2) scrutiny from a granting agency that might lead to a suspension of research or an adverse effect on future funding.⁶⁰

In order to enhance compliance with reporting requirements, barriers need to be identified, and targeted strategies need to be applied to remove those barriers. The literature identifies a number of barriers, including

- the lack of explicit standardized protocols;
- the lack of effective training on protocols;
- the lack of awareness that infection may have been laboratory-acquired;
- reporting systems that may have required individuals to pass through layers to reach the biosafety office (e.g., the supervisor, laboratory manager, or principal investigator);
- fear of punitive measures at the laboratory or institutional level;
- individual or institutional embarrassment;
- a poor relationship with medical support services (such as occupational safety and health services); and
- the lack of useful investigation/follow-up/feedback.

⁵⁹For additional information, see E.J. Baron and J. M. Miller, "Bacterial and Fungal Infections Among Diagnostic Laboratory Workers: Evaluating the Risks," *Diagnostic Microbiology and Infectious Diseases*, epub; D.L Sewell, "Laboratory-Associated Infections and Biosafety," *Clinical Microbiology Reviews*, Vol. 8, No. 3 (1995); R.M. Pike et al., "Continuing Importance of Laboratory Acquired Infections," *American Journal of Public Health*, Vol. 55, No. 2 (February 1965).

⁶⁰High-Containment Biodefense Research Laboratories, Meeting Report and Center Recommendations, *Biosecurity and Bioterrorism*, vol. 5, 1 (New Rochelle, N.Y., March 2007).

In addition, these incidents need to be analyzed so that (1) biosafety can be enhanced by shared learning from mistakes and (2) the public can be reassured that accidents are thoroughly examined and the consequences of an accident are contained. One possible mechanism for analysis discussed in the literature is the reporting system used for aviation incidents that is administered by the National Transportation Safety Board and the Federal Aviation Administration.⁶¹ When mistakes are made, they are analyzed and learned from without being attributed to any one individual. Although experts have agreed that some form of personal anonymity would encourage reporting, it is not clear how this mechanism would be applied to high-containment laboratories where, for example, one may not know about the exposure or whether the event is significant enough to be reported.

Compliance with Regulations Regarding Agent- and Experimental Task-Specific Training Is Needed to Ensure Maximum Protection

The select agent regulations require safety risk assessments whenever work with select agents is proposed. Risk assessments are of paramount importance because the investigator, management, and biosafety representatives must establish guidelines for safe, secure, and efficient research. Personnel working with select agents need training to ensure their own safety and that of coworkers and the surrounding community. Training is specifically designed to address select agent characteristics that include infectivity and pathogenicity. Training must also address hazardous operations such as intentional aerosolization, centrifugation, and homogenization. Some laboratories require inexperienced workers to be mentored by personnel experienced in containment procedures, a process that can take up to a year to complete. The mentor maintains a checklist of important operations that must be performed in a responsible manner before the worker will be allowed to work independently. Non-laboratory personnel who require access to high-containment laboratories (inspection, maintenance, and calibration staff) must also receive training that covers emergency response and agent-specific information.

If TAMU had provided effective, measurable staff training—including protocol-specific training on agent characteristics for *Brucella* (infectivity

⁶¹Department of Transportation, Federal Aviation Administration, *FAA Procedures for Handling National Transportation Safety Board Recommendations* (Washington, D.C., Federal Aviation Administration, March 22, 1995). Also see Federal Aviation Administration, *Accident and Incident Data* (Washington, D.C., Sept. 29, 2006).

and pathogenicity), common routes of infection, and medical signs and symptoms information—the worker might have been more aware of the dangers involved when cleaning the aerosol chamber and could have been protected from this exposure. Typical routes of infection differ for *M. tuberculosis* and *Brucella*, and normal procedures, including gowning and respiratory equipment, vary for the two agents. For example, the laboratory worker wore protective glasses, but they were not tight fitting. Experts told us that if procedures that are effective to avoid exposure to live virulent *M. tuberculosis* were being followed correctly, these should have been effective for *Brucella* despite the difference in the infectious dose.

According to an expert who has managed high-containment laboratories, there are risks involved in working alternately in BSL-2 and BSL-3 laboratories with their different levels of procedures and practices. Laboratory workers may develop a routine with BSL-2 procedures that may be difficult to consciously break when working with the more dangerous agents and activities requiring BSL-3 containment. Adequate training can help to minimize the risks involved.

Standardized Mechanisms for Informing Medical Providers about the Agents Laboratory Staff Work with Must Be Developed

Severe consequences for the worker can result from delays in (1) recognizing when an exposure has occurred or (2) medical providers accurately diagnosing any resulting infection. Further, if the worker acquires a disease that is easily spread through contact (direct physical and/or respiratory), there can also be severe consequences for the surrounding community.

According to the BMBL, the incidents causing most laboratory-acquired infections are often accidental and unknown. Those involved can conclude that an exposure took place only after a worker reports illness—with symptoms suggestive of a disease caused by the relevant agent—some time later. An infected person may be contagious for weeks until clinical symptoms become apparent. It is important that exposure be identified as soon as possible so that proper diagnosis and prompt medical treatment can be provided. To do so, medical providers need to be informed, in a standardized way, of all the agents that laboratory staff work with.

The issue of recognizing exposure and infection is not new, and organizations have put in place systems and procedures that, while not infallible, greatly facilitate such recognition. As part of the oversight

process, a review and evaluation of such procedures and their effectiveness are likely to be beneficial.

Current Confusion over the Definition of Exposure Needs to Be Addressed

According to our experts, a system that requires documentation of all accidental releases of select agents by whatever means and ensures that this information is available to the inspecting/oversight authority would provide both a valuable database and the foundation for any further investigation. Any accidental release in an area where unprotected personnel are present should then be considered a de facto exposure and be immediately reported to the oversight authority whether or not there is any resulting infection. Laboratory personnel who contract any infection, even if there is no evidence of exposure, should inform their physician about their work, including details of the specific agent(s) that they work with.

When we asked DSAT officials about the confusion over the definition of an exposure, they agreed that the terms need to be clearly defined and stated that they were drafting new guidance.⁶² DSAT officials noted, however, that it is unwise to wait until clinical symptoms appear before determining that an exposure has taken place, as this could potentially endanger a worker's life and, in the case of a communicable disease, the lives of others. A DOD and NIH expert on this issue told us that correctly interpreting the meaning of elevated titers—whose characteristics can vary by agent, host, and testing laboratory—is challenging since many serological testing methods have not been validated.

⁶²According to DSAT, their “concern was not necessarily with TAMU’s interpretation of the titers, but rather, that TAMU lacked an effective surveillance system. An elevated titer may result in the conclusion that the person was exposed to the agent. However, the entity must perform a follow-up investigation to determine if the elevated titer is the result of: (1) previous exposure to the organism prior to work at the entity; (2) possible exposure to the organism while doing non-work-related activities; or exposure at the workplace.”

To help clarify any confusion about what is considered a reportable theft, loss, or release, CDC released a new guidance document.⁶³ Scenario 20 in this document is an attempt to provide a simple approach by identifying three possible explanations for an elevated titer. However, it fails to go far enough and should state that an elevated titer of an agent that is being worked with in the laboratory should be regarded as prima facie evidence of exposure unless and until proved otherwise. Although clinical samples should then be taken at once to look for evidence of active infection, treatment of the person, as appropriate, should begin without delay to protect the health of the individual and, in some cases, safeguard the wider community.

Serological testing is an indirect diagnostic tool suggesting, but not proving, exposure to an agent and is typically used to direct follow-up with more conclusive tests. Because elevated titers can be due to reasons other than active infection with a particular agent, the results need to be treated with caution. Nevertheless, an elevated antibody titer in cases where that agent is being worked with in the laboratory must always be a matter of concern and action.

Serological testing is not definitive and scenario 20 does not provide clear guidance with regard to follow-up actions. Accordingly, standard operating procedures need to be developed by the institutions working together with biosafety officers/responsible officials and occupational health physicians to describe the appropriate course of action when elevated titers are observed.

The use of serological testing as a method to identify potential exposures to select agents must be approached with a high degree of caution. First, guidelines must be very clear regarding the intended use of any serology-based screening program. If routine screening indicates elevated antibody titers against a specific pathogen over baseline levels, it may suggest a laboratory exposure to a pathogen; however, alternative explanations are also feasible. The increase in titers may indicate natural exposure to the agent (depending on the agent and location of the laboratory). The increase could also result from inconsistencies associated with laboratory testing. Most serological assays for select agents are not commonly

⁶³This document is available on the National Select Agent Registry Web site: http://www.selectagents.gov/resources/CDC-APHIS_Theft_Loss_Release_Information_Document.pdf

conducted in clinical laboratories and are mostly performed in research laboratories. As such, these assays may not be properly controlled and validated. Assay-to-assay variation may be high, especially if experience is limited. Additionally, such assays are not particularly robust unless baseline specimens are available for comparison testing and serum samples are collected at relatively short intervals (for example, 3 to 6 months).

Similarly, a serological screening program used as a method to diagnose infection or prevent the spread of contagious pathogens to the community is unlikely to be successful unless samples are taken at short intervals, as elevated antibody titers are usually detected after the period of maximum contagiousness of most pathogens. Therefore, the most appropriate use for a serological screening program would be to identify past exposures and to facilitate remedial training or conduct retrospective risk analyses that might lead to improved risk mitigation procedures and policies that might prevent future exposures. It is critical that guidance on the use of blood screening programs clearly identify the purpose of these programs and also provide guidance on how information from these programs should be used. Any suspicion of exposure should be reported and investigated, and the result of that investigation should be reported, thus providing a complete picture for DSAT and reducing subjective bias in reporting.

The development of scientifically sound and standardized methods of identifying exposure is critical so that individual laboratory owners are not left to determine for themselves what is and what is not reportable. DSAT and APHIS could provide specific guidance on exposure benchmarks for each of the different select agents and toxins.

**Actions Taken by the
Regulatory Agency—DSAT—
Subsequent to the Incident**

On April 20, 2007, DSAT issued a cease-and-desist order suspending work with *Brucella* species at TAMU. On June 30, 2007, DSAT suspended all work with select agents at TAMU. The DSAT concerns included whether TAMU had a plan to prevent unauthorized access to select agents and toxins and a program that provided effective medical surveillance of occupational exposures to select agents and toxins. DSAT conducted a comprehensive site review and released a report in August 2007 that detailed a long list of safety violations, including instances in which the school did not immediately report or neglected to report laboratory worker infections or exposure to *Brucella* or *C. burnetii*. It also extended the suspension of research with select agents until the university addressed the issues in the August report.

HHS's Office of Inspector General (OIG) imposed a fine on TAMU for the select agent violations. The HHS OIG was delegated authority to impose civil monetary penalties of up to \$250,000 against an individual and up to \$500,000 against any other person, including any entity.⁶⁴ The HHS OIG and TAMU disagreed on the number of violations. In February 2008, TAMU agreed to pay a \$1 million fine, which was an unprecedented amount for a fine paid by any institution under the select agent program.

Incident 3: Power Failures at CDC's High-Containment Laboratories

Continuity of electrical power is vital for the safe functioning of high-containment laboratories, in particular since maintenance of essential pressure differentials using electrically driven fans provides an important barrier for preventing the uncontrolled release of agents.⁶⁵ Lapses in electrical power that occurred at a CDC laboratory raise concerns about standards in high-containment laboratory facility design, management of construction, and operations.⁶⁶

On June 8, 2007, the CDC campus in Atlanta experienced lightning strikes in and around its new BSL-4 facility, and both the Georgia Power-supplied primary power and CDC-supplied backup power from its centrally-located

⁶⁴42 U.S.C. § 262a(i) (Bioterrorism Act); 42 C.F.R. § 73.21.

⁶⁵For ease of reading, we have chosen not to include technically detailed descriptions of CDC's primary and backup power systems. For further information concerning the general requirements of backup power, please see (1) National Fire Protection Association, NFPA 70, National Electric Code 2008 Edition (Quincy, MA) (a) "Article 700 Emergency Systems;" (b) "Article 701 Legally Required Standby Systems;" and (c) "Article 702 Optional Standby Systems" and (2) National Fire Protection Association, NFPA 110, Standard for Emergency and Standby Power Systems 2005 Edition (Quincy, MA).

⁶⁶In commenting on our draft report, CDC stated that lapses in electrical power are highly likely regardless of the cause and type of laboratory or facility being served. CDC, as a result, employs an integrated approach combining laboratory procedures/training, health and safety protocols, and engineering/facility controls. CDC stated that the BMBL treats engineering controls for high-containment laboratories as secondary containment.

generator plant were unavailable.⁶⁷ The high-containment laboratory facility, not operational at the time, was left with only emergency battery power—which can provide limited electrical power for functions such as emergency lighting to aid in evacuation. Among other things, the outage shut down the high-containment laboratory’s negative air pressure system.⁶⁸ While investigating the power outage, the CDC later determined that, some time earlier, a critical grounding cable buried in the ground outside the building had been cut by construction workers digging at an adjacent site. The cutting of the grounding cable, which had hitherto gone unnoticed by CDC facility managers, compromised the electrical system of the facility that housed the BSL-4 laboratory.⁶⁹ With the grounding cable cut, the lightning strikes caused the circuit breakers in the building’s switchgear to disengage or open, resulting in a loss of primary power to the building. In addition, when the circuit breakers disengaged, the CDC’s backup generators were electrically isolated from the building and could not supply the building with power. It took approximately an hour for the CDC facility staff to reset the circuit breakers in the building to reengage the primary power.

Because of the June 2007 power outage incident, questions about the design of the backup power system for the new facility resurfaced. When the CDC designed the backup power system for the new BSL-4 facility, it decided to use diesel generators centralized at CDC’s utility plant that also

⁶⁷In commenting on our draft report, CDC stated that “as a consequence of the lightning strike, building 18 immediately experienced a blackout except for areas served from the uninterruptible power system (UPS) for the building. CDC operational staff immediately responded to the loss of power by following operational protocols that require the operator to investigate the possible cause of power loss and resetting over-current devices, if necessary, to restore normal or backup power, if required, to the building. After performing a brief survey of building systems and areas, CDC operational staff proceeded to the electrical switchgear room located on the triple sub-basement of building 18. CDC operational staff noticed that both 480 main breakers for the building were in a tripped status. The operator attempted to manually reset both tripped main breakers without success, whereupon the operator determined both breakers were restricted-open per system safety interlock. Upon further analyses and review, CDC determined that both main breakers tripped on ground fault current in excess of set limits. After a thorough review of the electrical system, the main breakers were reset and power was restored at the building in approximately 1 hour.”

⁶⁸The laboratory’s negative air pressure system is fan-operated and is designed to prevent potentially contaminated air from leaving the lab without first being treated to neutralize the contamination.

⁶⁹A subsequent third-party investigation determined that the grounding of another building housing CDC’s older BSL-4 laboratories was also compromised in a similar fashion.

serve other facilities, as well as functions such as chillers, on the campus. According to internal documents provided to us, during the design phase for the facility, some CDC engineers had questioned the choice of this remotely placed, integrated design rather than a simpler design using local backup generators near the BSL-4 facility.

According to CDC facility officials, the full backup power capabilities for the new BSL-4 facility were not in place at the time of the power outage but were awaiting completion of other construction projects on campus. Once these projects are completed, these officials said, the new BSL-4 facility will have multiple levels of backup power, including the ability to get power from a second central utility plant on campus, if needed. But some CDC engineers that we talked with questioned the degree of complexity in the design. They worried that an overly integrated backup power system might be more susceptible to failure. As a result of the power outage, CDC officials conducted a reliability assessment for the entire campus power system, which included the backup power design for the new BSL-4 facility. CDC concluded that its existing centrally located generators and planned power-related construction projects with equipment upgrades were more reliable and cost-effective than scenarios that locate generators at individual buildings.

CDC officials reported that its backup power system is tested monthly, as required by building code. In commenting on our draft report, CDC provided studies and data that showed the theoretical reliability of the power system. However, CDC could not provide us documentation of actual non-testing instances where the backup generator system operated as designed. This incident highlighted the risks inherent in relying on standard building codes to ensure the safety of high-containment laboratories—as there are no building codes and testing procedures specifically for high-containment laboratories.

In a second incident, on Friday January 4, 2008, CDC officials told us that nearby construction again damaged the grounding system of the building containing the new BSL-4 facility. The damage was observed when it occurred, but the cable was not repaired until the following week. While there was no loss of power to the BSL-4 facility, the potential for repeating a grounding-related power failure existed until repairs were made.

According to CDC officials, at the time of both incidents, the new BSL-4 facility in building 18 was in preparation to become fully operational. No laboratory work of any kind had been conducted inside the BSL-4 laboratories, and no live agents were inside the facility as the

commissioning process was still ongoing and the laboratories were not activated. However, given that the grounding cables were cut, it is apparent that the building's integrity as it related to adjacent construction was not adequately supervised. Further, according to CDC officials, standard procedures under building codes do not require monitoring of the integrity of the electrical grounding of the new BSL-4 facility. CDC has now instituted annual testing of the electrical grounding system as the result of its review of these incidents.⁷⁰

According to CDC officials, a third incident occurred on July 11, 2008, when a bird flew into the high voltage side of one of the Georgia Power transformers on the CDC campus, causing a failure in the primary electrical power supplied to buildings containing BSL-3 facilities. The CDC's backup generators did not provide power because of the cascading effects of a failure by one of the generators. As in the June 2007 incident, the facilities were left with only temporary battery power, shutting down the fans powering the facility's negative air pressure system. The generator problems were corrected by CDC in approximately an hour, at about the same time that Georgia Power completed its repairs and primary electrical power was restored.⁷¹

**Lessons Learned: BSL -3 and -4
Laboratory Safety Measures
Must Be Commensurate with
the Level of Risk These
Laboratories Present**

In any workplace building—regardless of the nature of its activities—there are safety features to protect the physical safety of workers. Various building codes cover many aspects of building design and construction required to achieve this safety objective, but the codes are subject to local interpretation. In general, the building codes enable (1) personnel to safely evacuate and (2) rescue personnel or firefighters to perform their jobs. By definition, additional hazards beyond those anticipated by standard building codes potentially exist in high-containment laboratories (BSL-3

⁷⁰In commenting on the draft report, CDC stated that while directional airflow and negative pressure in BSL-4 laboratories are crucial engineering components of a normal "safe" operating environment, engineering systems do fail from time to time for various reasons. Therefore, CDC relies on a "three-legged" approach to biocontainment (combining laboratory procedures/training, health and safety protocols, and engineering controls) to ensure that material is not released outside. Details on CDC's approach are included in appendix VI. We agree that the three-legged approach offers multiple layers of containment; however, CDC does not address the point we are making about the weaknesses we have identified in its electrical system.

⁷¹Power failures can also occur intentionally. We reported in 2003 on suspicious power failures at a high-containment laboratory working with foreign animal diseases. See [GAO-03-847](#), 20-21.

and BSL-4), and they are addressed in BMBL. However, according to CDC and NIH, BMBL is only advisory.

BMBL contains principles and guidelines, but the document does not provide specific detail on how functional requirements are to be translated into design solutions. According to our experts, there have been instances where modifications to laboratories were required after construction to achieve the necessary compliance. A more active, early, and continuing dialogue between builders, operators, and regulators may be beneficial in avoiding such waste and is especially relevant where tax dollars are committed to the creation or upgrading of high-containment laboratories.

Because BMBL addresses issues relating to maintaining the containment of biological agents to protect both workers and the wider public, its guidelines are potentially more restrictive than the building codes. According to our expert panel, a clear and unambiguous set of standards stating the various capabilities that are required to maintain the integrity of all high-containment laboratories is necessary. Such a set of standards will need to integrate building codes with the BMBL provisions or amendments thereto. These standards should be national—not subject to local interpretation—and address the possibility that one or more emergency or backup systems may fail. Most importantly, any set of scenarios aimed at maintaining containment integrity must be empirically evaluated to demonstrate its effectiveness. Adequate oversight of any nearby activities—such as adjacent construction with its potential to compromise buried utilities—must also be taken into consideration when evaluating the safety measures required to manage the risks of high-containment laboratories.

The CDC's BSL-4 laboratory was designed with multiple layers of electrical power so that if primary power failed, a secondary source of power would be in place for continuity of operations. Failure to monitor the system's integrity, however, compromised the ability of either power source to support critical operations. The power outages at CDC demonstrate a need to create understanding throughout the organization that effective biosafety involves layers of containment and, furthermore, that the loss of any one layer is serious even though the remaining layers, as intended, do maintain containment. Thus, procedures are required to regularly assess the functional integrity of every layer of containment and to initiate immediate corrective actions as required. The fact that taken as a whole, containment is being maintained is not a sufficient measure of system integrity: each component must be individually assessed and its operational effectiveness validated on a regular schedule.

Actions Taken by the
Regulatory Agency—DSAT—
Subsequent to the Incident

According to DSAT, since the CDC laboratory was not registered under the select agent regulations at the time of the incident, no DSAT action was required.⁷²

Incident 4: Release of
Foot-and-Mouth Disease in
the United Kingdom

High-containment laboratories are highly sophisticated facilities that require specialized expertise to design, construct, operate, and maintain. Because these facilities are intended to contain dangerous microorganisms, usually in liquid or aerosol form, even minor structural defects—such as cracks in the wall, leaky pipes, or improper sealing around doors—could have severe consequences. Supporting infrastructure, such as drainage and waste treatment systems, must also be secure.

In August 2007, foot-and-mouth disease contamination was discovered at several local farms near Pirbright in the U.K., the site of several high-containment laboratories that work with live foot-and-mouth disease virus. Foot-and-mouth disease is one of the most highly infectious livestock diseases and can have devastating economic consequences. For example, a 2001 epidemic in the U.K. cost taxpayers over £3 billion, including some £1.4 billion paid in compensation for culled animals.⁷³ Therefore, U.K. government officials worked quickly to contain and investigate this recent incident.

Lesson Learned: Facilities
Supporting High-Containment
Laboratories Must Ensure the
Operational Effectiveness of
Physical Infrastructure

The investigation of the physical infrastructure at the Pirbright site found evidence of long-term damage and leakage of the drainage system servicing the site, including cracked and leaky pipes, displaced joints, debris buildup, and tree root ingress. While the definitive cause of the release has not been determined, it is suspected that contaminated waste water from Pirbright's laboratories leaked into the surrounding soil from the deteriorated drainage pipes and that live virus was then carried off-site by vehicles splashed with contaminated mud.

⁷²On May 27-30, 2008, DSAT inspected this laboratory, which included a review of the incident response plan in the event of a power outage. On October 8, 2008, DSAT approved this laboratory for registration.

⁷³See Department for Environment, Food, and Rural Affairs, *Foot and Mouth Disease: Applying the Lessons* (London, U.K., National Audit Office, Feb. 2, 2005). We also reported on this 2001 U.K. incident. See GAO, *Foot and Mouth Disease: To Protect U.S. Livestock, USDA Must Remain Vigilant and Resolve Outstanding Issues*, [GAO-02-808](#) (Washington, D.C.: July 26, 2002).

The cracked and leaky pipes found at Pirbright are indicative of poor maintenance practice at the site. The investigation found that (1) monitoring and testing for the preventive maintenance of pipe work for the drainage system was not a regular practice on-site and (2) a contributing factor might have been a difference of opinion over responsibilities for maintenance of a key pipe within the drainage system.

High-containment laboratories are expensive to build and expensive to maintain. Adequate funding for each stage needs to be addressed. Typically, in large-scale construction projects, funding for initial construction comes from one source, but funding for ongoing operations and maintenance comes from another. For example, NIAID recently funded 13 BSL-3 laboratories as regional biocontainment laboratories (RBL) and 2 BSL-4 laboratories as national biocontainment laboratories (NBL). According to NIAID, it contributed to the initial costs for planning, design, construction, and commissioning and provided funding to support the operation of these facilities. For these laboratories, the universities are partially responsible for funding maintenance costs.⁷⁴

The Pirbright incident shows that beyond initial design and construction, ongoing maintenance plays a critical role in ensuring that high-containment laboratories operate safely and securely over time. Because even the smallest of defects can affect safety, ensuring the continuing structural integrity of high-containment laboratories is an essential recurring activity.

The failure of part of the physical infrastructure at the U.K.'s Pirbright facility and the outbreak of foot-and-mouth disease highlight the importance of ongoing maintenance of such facilities, together with clear lines of responsibility regarding shared infrastructure facilities. In addition, this incident and other incidents emphasize the importance of regulators and laboratories working in partnership to either ensure that funding to maintain the infrastructure is available or alter work programs and eliminate activities that cannot be performed safely.

⁷⁴In commenting on our draft report, NIAID noted that the cooperative awards were made to the NBLs in fiscal year 2006 to "develop and maintain the research resources and facilities needed to meet national, regional, and local biodefense and emerging infectious diseases research needs." NIAID plans to continue support for these awards.

Actions Taken by the U.K. Regulatory Agency Subsequent to the Incident

Since the outbreak of foot-and-mouth disease originating from Pirbright, a number of regulatory decisions have been made:

1. The U.K. government undertook a review of the regulatory framework governing work with animal pathogens that resulted in a November 2007 report. The government accepted all the report's recommendations, which included (1) moving regulation of work with animal pathogens from Defra to HSE and (2) developing a single regulatory framework covering work with human and animal pathogens based on the model provided by the Genetically Modified Organisms (Contained Use) Regulations 2000. This framework adopts a risk-based approach to regulation.
2. The Specified Animal Pathogens Order (SAPO) was amended in April 2008 to give inspectors increased powers, including the power to serve improvement and prohibition notices on entities (called duty holders in the U.K.) to remedy poor standards in such areas as containment and management. At the same time, HSE entered into an agency agreement with Defra to inspect premises where work with SAPO agents is carried out before Defra issues licenses; the license conditions are based on recommendations from HSE. Furthermore, HSE inspectors investigate any accidents and also proactively inspect facilities to ensure compliance with the license conditions.
3. Both organizations at Pirbright (Institute for Animal Health (IAH) and Merial) had their licenses amended or withdrawn following the outbreak. The IAH license was amended to allow diagnostic work (in the epidemiology building) and a limited amount of research in the arbovirology building. No animal work has been licensed to date, although new animal house facilities are nearing completion, and work may be licensed later this year.
4. All the drainage systems on-site have been tested and relined, and a new dual containment system has been laid to connect laboratories to a refurbished heat treatment plant. This new system is not yet operational, although it is in the final stages of commissioning. In the meantime, no laboratory or manufacturing effluent is discharged to the relined drainage system unless it has been heat treated by autoclaving (IAH) or been through a validated heat treatment cycle (Merial). The only effluent going to the drain and to the final chemical treatment plant is shower water, which should not contain virus as all activities are carried out in cabinets or in enclosed systems.

-
5. A newly refurbished building on the IAH has recently been licensed to allow small scale research on a number of SAPO 4 viruses.
 6. Merial was fully relicensed following amendments to its procedures and joint Defra and HSE inspections. The new licenses are more detailed than the original versions and impose many more license conditions on the company.
 7. No enforcement action has been taken against either organization following the outbreak of foot and mouth disease. The enforcing body (part of the local council) decided that there was insufficient evidence to prosecute either IAH or Merial.

Conclusions

High-containment laboratories provide facilities that are needed for basic research, development of detection technologies, and diagnostic and medical countermeasures for biotreats. Accordingly, facilities are specialized and cannot easily be converted from one function to another. Medium- to long-term advance planning for the appropriate capacity levels is therefore essential, as is knowledge of existing capacity. Such advance planning needs to take into account the (1) projected future balance between biodefense and more traditional public health work, (2) the specific infectious disease problems and targets that the expansion is meant to address, and (3) targets for the laboratory expansion's timetable or benchmarks as to when specific capacities need to be available. We were unable to identify any governmentwide strategic evaluation of these issues for high-containment laboratories.

Furthermore, since no single agency is in charge of the current expansion, no one is determining the associated aggregate risks posed by the expansion. As a consequence, no federal agency can determine whether high-containment laboratory capacity may now be less than, meet, or exceed the national need or is at a level that can be operated safely.

If an agency were tasked or a mechanism were established with the purpose of overseeing the expansion of high-containment laboratories, it could develop a strategic plan to (1) ensure that the number and capabilities of potentially dangerous high-containment laboratories are no greater or less than necessary, (2) balance the risks and benefits of expanding such laboratories, and (3) determine the type of oversight needed.

Such an agency or mechanism could analyze the biothreat problems that need to be addressed by additional BSL-3 and -4 laboratories, the scientific and technical capabilities and containment features that such laboratories need to have, how the laboratories should be distributed geographically, and how the activities of the laboratories would be coordinated to achieve intended goals.

Standards for several key issues have not been developed. The agency or mechanism responsible for overseeing the expansion of high-containment laboratories could also be responsible for coordinating with the scientific community to develop guidelines for high-containment laboratory design, construction, and commissioning and training standards for laboratory workers; providing definitions for exposure; developing appropriate inventory control measures; and providing guidance on the most efficient approach to personnel reliability programs.

The oversight agency or mechanism could also address issues related to the ongoing funding needs of high-containment laboratories. While NIAID has provided funding to build RBLs and NBLs, these laboratories are expected to compete for funding from NIH to sustain their research. It is unclear what will happen to these facilities, their trained personnel, and their technology if no such funding is available. Further, as these facilities and other high-containment laboratories age, adequate funding sources must be identified for upgrades and maintenance, or the risks that they pose may outweigh their benefits.

Once laboratories have been commissioned and begin operating, continuing maintenance and testing/validation programs are needed to ensure that operating standards and regulatory compliance are maintained. As facilities age, the costs of such programs will rise and are likely to consume an increasing proportion of budgets. Although this affects federal, industrial, and academic laboratories, the impact is likely to be greatest on academic laboratories. Although federal laboratories are subject to annual funding, they tend to have programs that have long-term commitments and are not usually subject to major changes even if principal investigators (scientists) relocate. Industrial laboratories exhibit similar stability of operations once they are committed to projects and programs. In all these cases, maintenance budgets are less tied to funding for research than are those of academic laboratories, which are highly dependent on research grant funding to support both infrastructure maintenance as well as research programs. Indeed, the two activities may compete for available money. Relocation of a principal investigator who is the recipient of research grant funding can create problems for the

institute in maintaining the laboratory facilities. Given the high costs of creating high-containment laboratories, consideration also needs to be given to the issue of their maintenance and support as distinct from funding for research activity.

The four incidents at USAMRIID, TAMU, CDC, and Pirbright exemplify a number of failures of systems and procedures that are meant, in combination, to maintain the biosafety of high-containment laboratories to protect laboratory workers and the public. DSAT and APHIS could examine these incidents and apply the lessons learned across the program.

These incidents have been described and analyzed in detail both because they are recent and because detailed information was available about the various factors involved. Unfortunately, the incidents and their causal factors are not unique, and the scientific literature contains information about many incidents occurring over decades that often involved similar factors and the failure to maintain adequate biosafety.

Overall, the safety record of high-containment laboratories has been good, although a number of weaknesses have become apparent over time. Consequently, along with expansion there needs to be a commensurate development of both operational and oversight procedures to address known deficiencies and, as far as practicable, proactively evaluate future risks.

Laboratory operators, in collaboration with regulators, need to develop and work through potential failure scenarios and use that information to develop and put in place mechanisms to challenge procedures, systems, and equipment to ensure continuing effectiveness.

Recommendations for Executive Action

We recommend that the National Security Advisor, in consultation with the Secretaries of Health and Human Services (HHS), Agriculture (USDA), Defense (DOD), and Homeland Security (DHS); the National Intelligence Council; and other executive departments as deemed appropriate identify a single entity charged with periodic governmentwide strategic evaluation of high-containment laboratories that will

(1) determine

- the number, location, and mission of the laboratories needed to effectively meet national goals to counter biotreats;

-
- the existing capacity within the United States;
 - the aggregate risks associated with the laboratories' expansion; and
 - the type of oversight needed

and (2) develop, in consultation with the scientific community, national standards for the design, construction, commissioning, and operation of high-containment laboratories, specifically including provisions for long-term maintenance.

We recommend that the Secretaries of HHS and USDA develop (1) a clear definition of exposure to select agents and (2) a mechanism for sharing lessons learned from reported laboratory accidents so that best practices—for other operators of high-containment laboratories—can be identified.

Should the Secretaries consider implementing a personnel reliability program for high-containment laboratories to deal with insider risk, we recommend that they evaluate and document the cost and impact of such a program.

Recognizing that biological agent inventories cannot be completely controlled at present, we also recommend that the Secretaries of HHS and USDA review existing inventory control systems and invest in and develop appropriate technologies to minimize the potential for insider misuse of biological agents.

Agency Comments and Our Evaluations

We obtained written comments on a draft of our report from the Secretaries of HHS and USDA. The Executive Office of the President: National Security Council did not provide comments. HHS and USDA concurred with our recommendations that were directed to them (see appendixes VII and VIII). HHS officials also provided general comments, including some concerns that are discussed in appendix VII. In addition, DOD, HHS, and USDA officials provided technical comments, which have been addressed in the body of our report, as appropriate.

We are sending copies of this report to the Executive Office of the President; the Attorney General; and the Secretaries of Agriculture, Defense, Health and Human Services, and Homeland Security. In addition, the report will be available at no charge on the GAO Web site at <http://www.gao.gov>.

If you or your staffs have any questions about this report, please contact me at (202) 512-2700 or kingsburyn@gao.gov or Sushil K. Sharma, Ph.D., Dr.PH, at (202) 512-3460 or sharmas@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this report. GAO staff who made major contributions to this report are listed in appendix IX.



Nancy Kingsbury, Ph.D.
Managing Director, Applied Research
and Methods

List of Requesters

The Honorable Joseph I. Lieberman
Chairman

The Honorable Susan M. Collins
Ranking Member
Committee on Homeland Security
and Governmental Affairs
United States Senate

The Honorable Henry A. Waxman
Chairman

The Honorable John D. Dingell, Jr.
Chair Emeritus

The Honorable Joe Barton
Ranking Member
Committee on Energy and Commerce
House of Representatives

The Honorable Bart T. Stupak
Chairman

The Honorable Greg Walden
Ranking Member
Subcommittee on Oversight and Investigations
Committee on Energy and Commerce
House of Representatives

The Honorable Darrell E. Issa
Ranking Member
Committee on Oversight and Government Reform
House of Representatives

The Honorable John F. Tierney
Chairman

The Honorable Jeff Flake
Ranking Member
Subcommittee on National Security and Foreign Affairs
Committee on Oversight and Government Reform
House of Representatives

The Honorable Daniel E. Lungren
Ranking Member
Subcommittee on Emerging Threats, Cybersecurity,
and Science and Technology
Committee on Homeland Security
House of Representatives

The Honorable Michael T. McCaul
Ranking Member
Subcommittee on Intelligence, Information Sharing
and Terrorism Risk Assessment
Committee on Homeland Security
House of Representatives

The Honorable David E. Price
Chairman
Subcommittee on Homeland Security
Committee on Appropriations
House of Representatives

The Honorable Richard Burr
United States Senate

The Honorable John Linder
House of Representatives

Appendix I: Scope and Methodology

To determine the extent of expansion in the number of high-containment laboratories and the areas experiencing growth, we interviewed agency officials and experts and reviewed documents provided by agencies and scientific literature. To determine which federal agency has the mission to track and determine the aggregate risks associated with the proliferation of BSL-3 and BSL-4 laboratories in the United States, we surveyed 12 federal agencies that are involved with these laboratories in some capacity—for example, research, oversight, or monitoring.

The survey requested information on whether the agency (1) has a mission to track the number of high-containment laboratories, (2) has a need to know the number of operating BSL-3 and BSL-4 laboratories, and (3) knows that number. The agencies that received our survey included the Department of Agriculture; the Department of Commerce; the Department of Defense; the Department of Energy; the Environmental Protection Agency; the Department of Health and Human Services, including the Centers for Disease Control and Prevention (CDC); the Department of Homeland Security; the Department of the Interior; the Department of Justice, including the Federal Bureau of Investigation; the Department of Labor, including the Occupational Safety and Health Administration; the Department of State; and the Department of Veterans Affairs. In addition, we sent our survey to intelligence agencies, including the Central Intelligence Agency, the National Counter-Terrorism Center, the Defense Intelligence Agency, and the Office of Intelligence Analysis within DHS.

To supplement existing information on the current number of BSL-3 and BSL-4 laboratories in the United States, we surveyed 724 individuals, who were identified through various open sources as knowledgeable contacts on biosafety laboratories, through a self-administered electronic questionnaire posted on the World Wide Web between April 2007 and May 2007. We obtained responses from 295 respondents, for an overall response rate of 41 percent. Several important limitations should be noted about our survey. First, the universe of BSL-3 and -4 laboratories is unknown. While we used multiple sources to develop our list of potential respondents, there are likely other laboratories that we were unable to identify. Second, there may be duplicate responses in cases where multiple persons responded to the survey for a single institution. The data from our questionnaire are sufficiently reliable to demonstrate that there are BSL-3 or -4 laboratories that do not work with select agents.

We also met with officials of the Division of Select Agents and Toxins and the Animal and Plant Health Inspection Service to gain additional

information about the expansion of high-containment laboratories. Finally, we reviewed documents these agencies provided, including pertinent legislation, regulations, and guidance, and reviewed scientific literature on risks associated with high-containment laboratories.

To develop lessons learned from recent incidents at four high-containment laboratories, we interviewed academic experts in microbiological research involving human, animal, and plant pathogens and conducted site visits at selected federal, civilian, military, academic, and commercial BSL-3 and BSL-4 laboratories, including the sites involved in the recent incidents. Specifically, we conducted site visits at CDC and Texas A&M University (TAMU); talked to United Kingdom officials at the Health Safety Executive and the Department for Environment, Food, and Rural Affairs; and reviewed documents and inspection reports.

To discuss the incidents at TAMU and CDC, we conducted site visits and interviewed the relevant officials. During our site visit to CDC, we interviewed relevant officials, including the officials of CUH2A, Inc.—the contractor who designed the backup power system for the new BSL-4 laboratory in Atlanta—as well as the expert hired by this firm to conduct the reliability study for the backup power system.

We conducted our work from September 2005 through June 2009 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

Appendix II: Expert Panel

The expert panel that reviewed this report comprised scientists with substantive expertise in microbiological and select agent research and the operations of high-containment laboratories. The following were the panel members:

Peter Emanuel, Ph.D.
Office of Science and Technology Policy
Executive Office of the President

Gigi Kwik Gronvall, Ph.D.
Center for Biosecurity of the University of
Pittsburgh Medical Center
University of Pittsburgh

George V. Ludwig, Ph.D.
U.S. Army Medical Research and Material Command
Ft. Detrick, Maryland

Jack Melling, Ph.D., *Retired*
U.K. Microbiological Research Authority
Porton Down, United Kingdom

Alan Jeff Mohr, Ph.D., *Retired*
Life Sciences Division
U.S. Army, Dugway Proving Ground
Tooele, Utah

Suresh D. Pillai, Ph.D.
Texas A&M University
College Station, Texas

Janet Shoemaker
American Society for Microbiology
Washington, D.C.

Appendix III: List of Select Agents and Toxins as of November 17, 2008

HHS Select Agents and Toxins

Abrin
Botulinum neurotoxins
Botulinum neurotoxin producing species of *Clostridium*
Cercopithecine herpesvirus 1 (Herpes B virus)
Clostridium perfringens epsilon toxin
Coccidioides posadasii/Coccidioides immitis
Conotoxins
Coxiella burnetii
Crimean-Congo haemorrhagic fever virus
Diacetoxyscirpenol
Eastern Equine Encephalitis virus
Ebola virus
Francisella tularensis
Lassa fever virus
Marburg virus
Monkeypox virus
Reconstructed 1918 Influenza virus ¹
Ricin
Rickettsia prowazekii
Rickettsia rickettsii
Saxitoxin
Shiga-like ribosome inactivating proteins
Shigatoxin
South American Haemorrhagic Fever viruses
 Flexal
 Guanarito
 Junin
 Machupo
 Sabia
Staphylococcal enterotoxins
T-2 toxin

Tetrodotoxin
Tick-borne encephalitis complex (flavi) viruses
 Central European Tick-borne encephalitis
 Far Eastern Tick-borne encephalitis
 Kyasanur Forest disease

¹ Reconstructed replication competent forms of the 1918 pandemic influenza virus containing any portion of the coding regions of all eight gene segments.

Omsk Hemorrhagic Fever
Russian Spring and Summer encephalitis
Variola major virus (Smallpox virus) and
Variola minor virus (Alastrim)
Yersinia pestis

USDA Select Agents and Toxins

African horse sickness virus
African swine fever virus
Akabane virus
Avian influenza virus (highly pathogenic)
Bluetongue virus (exotic)
Bovine spongiform encephalopathy
Camel pox virus
Classical swine fever virus
Ehrlichia ruminantium (Heartwater)
Foot-and-mouth disease virus
Goat pox virus
Japanese encephalitis virus
Lumpy skin disease virus
Malignant catarrhal fever virus (Alcelaphine herpesvirus type 1)
Menangle virus
Mycoplasma capricolum subspecies *capripneumoniae* (contagious
caprine pleuropneumonia)
Mycoplasma mycoides subspecies *mycoides* small colony (*MmmSC*)
(contagious bovine pleuropneumonia)
Peste des petits ruminants virus
Rinderpest virus
Sheep pox virus
Swine vesicular disease virus
Vesicular stomatitis virus (exotic): Indiana subtypes VSV-IN2, VSV-IN3
Virulent Newcastle disease virus²

Overlap Select Agents and Toxins

Bacillus anthracis
Brucella abortus

²A virulent Newcastle disease virus (avian paramyxovirus serotype 1) has an intracerebral pathogenicity index in day-old chicks (*Gallus gallus*) of 0.7 or greater or has an amino acid sequence at the fusion (F) protein cleavage site that is consistent with virulent strains of Newcastle disease virus. A failure to detect a cleavage site that is consistent with virulent strains does not confirm the absence of a virulent virus.

Brucella melitensis
Brucella suis
Burkholderia mallei (formerly *Pseudomonas mallei*)
Burkholderia pseudomallei (formerly *Pseudomonas pseudomallei*)
Hendra virus
Nipah virus
Rift Valley fever virus
Venezuelan Equine Encephalitis virus

**USDA Plant Protection and Quarantine (PPQ) Select Agents and
Toxins**

Peronosclerospora philippinensis (*Peronosclerospora sacchari*)
Phoma glycinicola (formerly *Pyrenochaeta glycines*)
Ralstonia solanacearum race 3, biovar 2
Schlerophthora rayssiae var *zeae*
Synchytrium endobioticum
Xanthomonas oryzae pv. *Oryzicola*
Xylella fastidiosa (citrus variegated chlorosis strain)

Appendix IV: Biological Agents Recommended for BSL-3 Containment That Are Not Select Agents

There are a number of biological agents causing severe illness or death that are not select agents. Some non-select-agents are recommended for work, research, and production safely under BSL-2 containment (BMBL, 5th Edition). These agents are listed in table 11. Several of these non-select-agents may require BSL-3 containment for specific reasons, including production of aerosols or large-scale production of these organisms (BMBL, 5th Edition). These agents are listed in table 12.

Table 11: Agents Requiring BSL-2 Containment, Rarely BSL-3 Containment

Agent	Disease
<i>Bordetella pertussis</i>	pertussis (whooping cough) ^a
<i>Neisseria gonorrhoeae</i>	gonorrhea
<i>M</i>	meningitis, septicemia
<i>Salmonella typhi</i>	typhoid fever ^a
Hepatitis B, C, D viruses	hepatitis B ^a , hepatitis C, hepatitis D
Human herpes virus	herpes simplex et al.
Lyssaviruses	rabies ^a
Retroviruses	HIV

Source: BMBL, 5th Edition.

^aThese agents currently have vaccines available to the public.

Table 12: Agents Typically Requiring BSL-3 Containment

Agent	Disease
<i>Chlamydia psittaci</i>	psittacosis
Hanta virus	Hanta virus pulmonary syndrome
<i>Mycobacterium tuberculosis complex</i>	tuberculosis
Non-contemporary human influenza Strains (H2N2)	H2N2 influenza
Lymphocytic choriomeningitis virus	aseptic meningitis, encephalitis
SARS coronavirus	SARS ^a
West Nile virus	"West Nile virus" encephalitis

Source: BMBL, 5th Edition.

^aCDC has proposed that this agent be added to the select agents and toxins list.

Appendix V: The Army's Requirements for High-Containment Laboratories in 2001

According to DOD officials, DOD did not have a policy document specific to biological select agents and toxins (BSAT) or high-containment laboratories in 2001.

In 2001, all U.S. Army high-containment laboratories working with select agents were registered with CDC (under 42 C.F.R. § 72.6). Army safety regulations in place at that time required the following:

1. A hazard analysis must be conducted to determine safety precautions, necessary personnel protection, engineering features, and procedures to prevent exposure for all agents. The Army utilized the risk analysis technique of maximum credible events, which examines the consequences of realistic worst-case scenarios.
2. Facilities must have standard operating procedures, training and proficiency requirements, medical surveillance, emergency preparedness procedures (including advance notification to local, state, regional, and federal emergency response personnel), hazard labeling, disposal and maintenance controls, and protective equipment for all work with agents.
3. Quarterly inspections for biosafety level (BSL)-1 and BSL-2 laboratories and monthly inspections for BSL-3 and BSL-4 laboratories must be conducted.
4. All mishaps must be reported and investigated. Medical surveillance of all workers present must begin immediately after a mishap.
5. Access control procedures were required to keep people not needed to operate biological laboratories from entering.
6. Federal, state, and local laws must be obeyed when transporting agents.
7. Components that contract out biological defense work must prepare written procedures that set guidelines for facilities, safety, inspections, and risk analysis. They were also required to monitor contractor performance in meeting safety requirements, which includes pre-award inspections, annual inspections of BSL-3 facilities and semiannual inspections of BSL-4 facilities, documentation of safety training programs, designation of an individual responsible for safety, and storage and disposal procedures. Contractors working at BSL-3 and BSL-4 facilities must prepare a plan for controlling laboratory mishaps.
8. Facilities must have published safety plans and monitoring procedures that they coordinated with federal, state, and local emergency services and

practiced with emergency groups. An occupational health program, including medical surveillance examinations, was also required.

9. The regulations also set out operational requirements, including laboratory techniques, based on biosafety level, and emergency procedures, such as establishing evacuation procedures and an emergency alarm system.
10. Facilities must abide by personal protective equipment requirements (based on biosafety level), decontamination and disposal requirements and shipping restrictions, and facility specifications based on biosafety level and engineering controls.

These regulations are located at 32 C.F.R., parts 626 and 627. Army pamphlet 385-69 also prescribes the minimum safety criteria and technical requirements and is used in conjunction with these regulations.¹ Additionally, since USAMRIID was designated a “restricted area” in 1995, a National Agency Check was also required for general unescorted access for all staff. The USAMRIID Special Immunizations Clinic provided baseline medical and occupational health evaluations of fitness to work in the laboratories and provided vaccines. Annual medical interviews, physical exams, and laboratory reassessments were conducted for changes in health, medication, and duties.

According to information provided to us by USAMRIID, security clearance was not and is not required to work in high-containment laboratories, and having a security clearance did not by itself allow access to high-containment laboratories. In 2001, there was no centralized requirement for inventory control and accountability. Individual scientists maintained their own stocks and accountability.

CDC’s regulations in 2001 (42 C.F.R. § 72.6) focused on the transfer of select agents and thus did not focus on personnel security or insider risk or inventory control of select agents. While Army regulations required that the consequences of realistic worst case scenarios be examined, insider risk was not considered in such examinations.

¹In 2007, Army regulation 385-10, the Army Safety Program, provided policies on safety that included biological safety.

Appendix VI: CDC's Integrated Approach to Biocontainment at High-Containment Laboratories

In commenting on the draft report, HHS officials stressed the importance of the Centers for Disease Control and Prevention's (CDC) integrated "three-legged approach" to biocontainment at high containment laboratories. They provided the following technical details of their biocontainment experiences.

"According to CDC officials, monitoring one-pass directional airflow through negatively pressurized containment zones, enclosed and separated by airtight doors and structure, with HEPA filtration on both the supply side (one HEPA filter) and the exhaust side (two HEPA filters), along with robust Operations and Maintenance protocols (O&M) provides a sound facility design and construction component for CDC's 'three-legged' approach to biocontainment. This approach, which is described in Section II of the BMBL, stresses that laboratory practice and technique is the most important element of a comprehensive containment strategy, in conjunction with appropriate safety equipment (as a primary barrier) and facilities design/construction and engineering (as a secondary containment barrier). CDC maintains that while directional airflow and negative pressure in BSL-4 laboratories is a critical engineering component of a normal 'safe' operating environment, engineering systems do fail from time-to-time, for various reasons.

"In the event of a loss of power to the supply and exhaust fans and controls that maintain negative pressure conditions in CDC's BSL-4 laboratories, the laboratories go to a 'static pressure' status, whereby secondary containment is maintained by the airtight door gaskets, airtight construction of interior walls, floors, and ceiling within the BSL-4 laboratory block, and because the HEPA filters on the supply side and exhaust ducts are functionally impermeable to air for certain periods of time under static pressure conditions. In effect proper design, construction and O&M render the CDC BSL-4 laboratories into airtight boxes during a complete loss of normal and standby power during these events. Containment was also preserved because CDC's laboratorians are properly trained in safe laboratory practices and procedures, and BSL equipment and safety protocols (primary barriers) functioned as intended. Equipment within the BSL-4 laboratories include biological safety cabinets, centrifuges, and heavy-duty personal protective suits (i.e., 'space suits').

"In the lightning and bird strike incidents outlined above [see pp. 58-61], secondary engineering controls failed due to temporary construction-related impacts, rather than typical operations conditions, and all but UPS-generated life safety required power was lost in B [building] 18. However,

because CDC had appropriated and effective laboratory practice and safety equipment and practices in place, and because a static pressure condition had been maintained (as a secondary barrier), the chance of an accidental release of dangerous pathogens into the environment so as to cause a significant risk to CDC workers or the surrounding community did not exist.

“According to CDC officials, the lightning and bird strike incidents are not typical of O&M-related incidents that CDC has experienced over the years since they are directly related to the intense construction activities at the Roybal Campus that have been ongoing since approximately 2000, and are expected to largely conclude in approximately 2011. The construction activities are the execution of the Agency’s 10-Year Master Plan to replace the many 50-year old buildings, including laboratories and infrastructure at the Roybal and Chamblee Campuses. CDC data [data] indicates that even with the lightning and bird strike incidents, the Roybal Campus electrical distribution system has had a 99.9997 percent reliability rate, or approximately 10 hours of documented down-time due to power outages during 78,840 hours of total run time (2000-2008). CDC expects to reduce electrical system downtime once construction activities have ceased.”

Appendix VII: Comments from the Department of Health and Human Services

Note: GAO comments supplementing those in the report text appear at the end of this appendix.



DEPARTMENT OF HEALTH & HUMAN SERVICES

OFFICE OF THE SECRETARY

Assistant Secretary for Legislation
Washington, DC 20201

JUL 20 2009

Nancy Kingsbury, Ph.D.
Managing Director
Applied Research and Methods
U.S. Government Accountability Office
441 G Street N. W.
Washington, DC 20548

Dear Ms. Kingsbury:

Enclosed are comments on the U.S. Government Accountability Office's (GAO) report entitled: "HIGH-CONTAINMENT LABORATORIES: Coordinated National Oversight is Needed" (GAO-09-574).

The Department appreciates the opportunity to review this report before its publication.

Sincerely,

Barbara Pisaro Clark
Acting Assistant Secretary for Legislation

Attachment

GENERAL COMMENTS FROM THE DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) ON THE GOVERNMENT ACCOUNTABILITY OFFICE'S (GAO) DRAFT REPORT ENTITLED, "HIGH-CONTAMINMENT LABORATORIES: COORDINATED NATIONAL OVERSIGHT IS NEEDED" (GAO-09-574)

The Department of Health and Human Services (HHS) thanks GAO for the opportunity to review and comment on this draft report. HHS concurs with GAO's recommendations that have been directed to the Secretary of HHS and respectfully submits the following comments about the report.

Knowing the Total Number of All BSL-3 Laboratories Could be Beneficial But Has Not Been Mandated

See comment 1.

In the section titled, "BSL-3 Labs Are Being Built in All Sectors Throughout the United States," GAO implies that the Centers for Disease Control and Prevention (CDC) should know the total number Biosafety Level-3 laboratories (BSL-3 laboratories) in the United States. Though it could be beneficial to know where all the BSL-3 laboratories are located across the country, it is important to point out prominently in this report that there is no executive or legislative mandate directed at any federal agency to know this information. The select agent programs at CDC and the United States Department of Agriculture (USDA)/Animal and Plant Health Inspection Service (APHIS) know the identity and location of all laboratories (BSL-2, BSL-3, and BSL-4) that possess, use, or transfer select agents, which is a tremendous data resource. They maintain this information because it was required by the Public Health Security and Bioterrorism Preparedness and Response Act of 2002. However, there is no such reporting requirement for laboratories that do not work with select agents. Knowing information about the location of all BSL-3 laboratories could be beneficial, but instituting new regulatory reporting requirements possibly could create a burden on private sector laboratories and would require new federal resources. To this end, HHS will recommend to appropriate entities to engage in a more in-depth policy debate on this issue.

See comment 2.

Suggestions for Presenting Information About Power Outages at CDC

See comment 3.

Because it does not appear that the report includes some important details that were provided in previously submitted responses, comments, and other written documents, HHS does not concur with GAO's assessment of Incident 3 and GAO's related findings.

We urge GAO to point out that the lightning strike that occurred on June 8, 2007 on CDC's campus affected BSL-4 laboratories that were not yet operational; no laboratory work of any kind had been conducted inside the BSL-4 laboratories in Building 18 prior to the lightning strike incident. In addition, no infectious pathogens were stored in this space because the commissioning process was still ongoing and the laboratories were not yet activated. It is important to note that there was never a threat to any laboratory workers, CDC employees, or the public. Conveying this information is critical so that readers will have a clear understanding about the outage.

We also urge GAO to note that even if the laboratories had been operational, there still would not have been any threat of exposure to any laboratory workers, CDC employees, or the public. The draft report currently does not discuss a very important facility design approach that ensures biocontainment, which is an approach that is embraced by CDC and implemented in the design and operations of the Building 18 high-containment laboratory. This approach is the "multi-tiered," or integrated "three-legged" containment, method that stresses three components: (1) laboratory practice and technique; (2) appropriate safety equipment as a primary containment barrier; and (3) facilities design, construction, and engineering as a secondary containment barrier.

GENERAL COMMENTS FROM THE DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) ON THE GOVERNMENT ACCOUNTABILITY OFFICE'S (GAO) DRAFT REPORT ENTITLED, "HIGH-CONTAMINMENT LABORATORIES: COORDINATED NATIONAL OVERSIGHT IS NEEDED" (GAO-09-574)

The approach, which is described in Section II of *Biosafety in Microbiological and Biomedical Laboratories 5th edition* (BMBL), stresses that laboratory practices and techniques are the most important elements of a comprehensive containment strategy. CDC maintains that all three components are necessary when analyzing the effectiveness of biocontainment in BSL laboratories and that no single component failure will *necessarily* constitute the loss of containment. Although this detail was covered during meetings with GAO and would be beneficial to include, this information is not currently reflected in the report.

See comment 4.

We do question GAO's assessment that problems with primary power failures of BSL-4 laboratories could have "devastating consequences" (Lessons Learned section for Incident 3). Because it is unclear how GAO defines "devastating," it may be overstating the problem about the impact of a loss of power. All air in a BSL-4 laboratory is filtered before entering both the inside and outside environments and the workers in the laboratory are protected from aerosols through the positive pressure suits or sealed biological safety cabinets. Please note that the systems are designed to maintain containment, and many system components are redundant and overlapping. Thus, the loss of one component does not necessarily result in loss of overall containment.

See comment 5.

Also, the draft report should include several important details regarding the critical differences, purpose, and functions differentiating code-required emergency power and legally required standby power. These differences are important when planning and designing electrical distribution systems for biological laboratories and other science buildings and should be carefully considered when performing an analysis of such a system. Comments and other written data concerning this topic were provided to GAO.

Serological Testing Can Indicate an Exposure if Interpreted Properly

In discussing the Texas A&M University incident, the GAO report addresses the issue of using serological testing to monitor potential exposures to select agents. When used properly, serological testing can be an effective method for detecting exposures to infectious agents, including select agents. A serum titer that is higher than a baseline titer is not necessarily considered an exposure. The rise in titer is the most important aspect of identifying infection, assuming that a pre-exposure serum is also tested. The titer should be at least 4 times higher than a baseline to be considered an exposure, and the timeframe in which the testing was done (relative to the baseline) is also important. Antibody titers generally rise *after* clinical symptoms appear. Many nuances to the proper interpretation of serological testing exist (e.g., the appropriate use and interpretation of these tests; and identification of type of antibody [IgM and IgG]). All of these factors need to be considered to best interpret serological testing. Before finalizing findings and conclusions on this issue, GAO may find it helpful to get assistance from specialists in serological testing.

See comment 6.

The report also indicates that more guidance is needed for the regulated community in using this method. CDC and APHIS jointly developed the *Select Agents and Toxins Theft, Loss and Release Information Document* to provide guidance to the regulated community on what constitutes an occupational exposure to a select agent, including guidance on the interpretation of serological testing (http://www.selectagents.gov/resources/CDC-APHIS_Theft_Loss_Release_Information_Document.pdf).

GENERAL COMMENTS FROM THE DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) ON THE GOVERNMENT ACCOUNTABILITY OFFICE'S (GAO) DRAFT REPORT ENTITLED, "HIGH-CONTAMINMENT LABORATORIES: COORDINATED NATIONAL OVERSIGHT IS NEEDED" (GAO-09-574)

However, the *Select Agents and Toxins Theft, Loss and Release Information Document* is not the only tool used by the HHS and USDA select agent programs to communicate with registered entities on occupational health issues such as serological testing: As part of the oversight process, select agent programs routinely review occupational health plans. In addition, select agent liaisons are routinely available to discuss occupational health issues with responsible officials and other members of the regulated community.

Recommendations for the National Security Advisor

HHS is committed to working with the National Security Advisor should a government-wide, strategic evaluation of high-containment laboratories be undertaken.

To inform this discussion, we note that national goals to counter biotreats may change over time. Laboratories are built to last 50 years or longer, so assessing whether current laboratory capacity will be appropriate for future needs is difficult. A BSL-3 laboratory can be used for BSL-2 work, but it is impossible, without renovating it, to use a BSL-2 laboratory for BSL-3 work. Therefore, it is more desirable to build for the maximum biosafety containment that is anticipated (e.g., BSL-3) while using a realistic estimate for future needs (e.g., more than 50 years). Otherwise, it would be impossible to work with highly pathogenic microorganisms—such as severe acute respiratory syndrome (SARS)—quickly. One may need to reconsider the suggestion that an oversight organization could address the needs and distribution of laboratories, and coordinate the intended goals, because the needs will change yearly. Coordination may not be easy because federal agencies have different agendas, timelines, and budgets.

The issue of how many laboratories should exist and where these laboratories should be located is complex. It is important to consider the uses of such laboratories in the future. For example, having a BSL-3 laboratory available in an institution is considered a bonus when it needs to be used quickly for new and emerging needs such as SARS. It is essential to have laboratory capacity for optimizing emergency response and public health threats. However, the overall need should be determined by taking into account the ability to respond effectively and quickly to natural and manmade infectious-disease emergencies across a wide region or area; the ability to create new science around the identification, characterization, and control of re-emerging or novel infectious-disease threats; and the ability to quickly develop appropriate countermeasures.

This report may not identify all gaps in high-containment laboratory facilities in clinical settings, including large community hospitals and tertiary-care facilities. Many believe that these types of clinical facilities often have inadequate containment measures for certain high-risk work. Expansion of laboratories does not automatically mean that too many laboratories exist, nor does it mean that the distribution and supply of existing high-containment laboratories is adequate or optimum. Any future evaluations of capacity and supply should examine the needs of the clinical laboratories related to their high-containment capacity.

GAO recommends that the National Security Advisor identify a single entity to evaluate high-containment laboratories. This entity should not only validate the number and capacity of the laboratories (to determine whether these factors are appropriate and meet the needs of the country), but identify the risks and determine what kind of oversight is needed.

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See comment 7.

See comment 8.

See comment 9.

GENERAL COMMENTS FROM THE DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) ON THE GOVERNMENT ACCOUNTABILITY OFFICE'S (GAO) DRAFT REPORT ENTITLED, "HIGH-CONTAMINMENT LABORATORIES: COORDINATED NATIONAL OVERSIGHT IS NEEDED" (GAO-09-574)

Regarding the concern of risks associated with expanding high-containment laboratories and their resulting capacity, such risks should be carefully balanced by (1) the rewards associated with the enhanced epidemiology and surveillance capacity; (2) the improved ability to respond to emergencies; and (3) the improved ability to mitigate outbreaks and control infectious diseases.

An amazing success story is the expansion of the Laboratory Response Network (LRN) during the past decade: now all 50 states, the District of Columbia, and several territories have BSL-3 capabilities. This development has been crucial in ensuring a safer and more robust response capability, and it has clearly enhanced our ability to identify, characterize, and respond to public health threats. Specifically, the LRN has greatly enhanced our response to seasonal influenza, H5N1, SARS, white-powder and toxin events, threat letters, and novel H1N1 influenza A virus.

GAO also recommends that there be a government-wide effort to develop national standards for designing, constructing, commissioning, and operating high-containment laboratories. Some national standards for design, construction, commissioning, and operation of these laboratories have been included in the BMBL. However, it may be more beneficial to share lessons learned in the trade than to create standards, which may not apply in all situations. In addition, many of these laboratories are already constructed and being maintained, so it would need to be determined how such standards would apply to them.

Recommendations for the Secretary of HHS

GAO Recommendation: We recommend that the Secretaries of HHS and USDA develop (1) a clear definition of exposure to select agents; and (2) a mechanism for sharing lessons learned from reported laboratory accidents so that best practices can be identified and shared with other operators of high-containment laboratories.

HHS Response: HHS agrees that it is important for select-agent registered entities to have a clear understanding of what constitutes an exposure to select agents. CDC's and APHIS' select agent programs have seriously considered the issue of select agent exposures. The APHIS/CDC *Select Agents and Toxins Theft, Loss and Release Information Document* that was published on January 18, 2009, contains a definition for occupational select agent exposures (http://www.selectagents.gov/resources/CDC-APHIS_Theft_Loss_Release_Information_Document.pdf). This definition, which is derived from the occupational exposure definition in the OSHA Bloodborne Pathogens Standard (29 CFR Part 1910-1030b), is as follows:

“Occupational exposure: Any event which results in any person in a registered entity facility or lab not being appropriately protected in the presence of an agent or toxin. This may include reasonably anticipated skin, eye, mucous membrane, or parenteral contact with blood or other potential infectious materials that may result from the performance of a person's duties. For example, a sharps injury from a needle being used in select agent or toxin work would be considered an occupational exposure.”

See comment 10.

GENERAL COMMENTS FROM THE DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) ON THE GOVERNMENT ACCOUNTABILITY OFFICE'S (GAO) DRAFT REPORT ENTITLED, "HIGH-CONTAINMENT LABORATORIES: COORDINATED NATIONAL OVERSIGHT IS NEEDED" (GAO-09-574)

The *Select Agents and Toxins Theft, Loss and Release Information Document* will also assist the regulated community in analyzing incidents for select agent exposures. Through 20 possible scenarios, it describes how this definition is applied to incidents that may occur in select agent facilities. We will review the *Select Agents and Toxins Theft, Loss and Release Information Document* and consider adding the occupational health response recommendations in Scenario 20.

HHS also agrees that lessons learned from laboratory accidents should be synthesized and shared with the broader laboratory community. The APHIS/CDC Form 3 collects information on thefts, losses, and releases of select agents. CDC will work with APHIS to synthesize the data that have been gathered about releases in laboratories registered with the select agent programs, and it will publish and share this analysis in a public report. Please note that HHS and USDA have the ability to gather such data only for laboratories that work with select agents. A separate mechanism must be identified to gather information about releases in laboratories that do not work with select agents.

GAO Recommendation: Should the Secretaries consider implementing a personnel-reliability program for high-containment laboratories to address insider risk, we recommend that they evaluate and document the cost and impact of such a program.

HHS Response: HHS agrees that there must be a careful analysis of the costs, risks, and benefits of personnel-reliability programs before such a requirement is instituted for the select agent program. The Working Group on Strengthening the Biosecurity of the United States, established by Executive Order 13486 and signed by President George W. Bush on January 9, 2009, also addresses this issue. The draft report was provided to the White House on July 9, 2009. HHS will work with its partners at USDA to carefully evaluate the value, feasibility, cost, and impact of implementing such a program. As part of the evaluation, HHS and USDA will consider the recommendations from this working group regarding personnel-reliability programs.

GAO Recommendation: Recognizing that biological agent inventories cannot be completely controlled right now, we also recommend that the Secretaries of HHS and USDA review existing inventory-control systems and invest in and develop appropriate technologies to help minimize the potential risk for an insider to misuse biological agents.

HHS Response: HHS agrees that inventory-control systems must be improved to minimize the potential risk for an insider to misuse biological agents. The Select Agent Regulations include requirements related to maintaining inventory logs of select agents. However, some have called for additional guidance from the select agent programs on requirements related to working stocks versus select agents that are held long term in storage. CDC's and APHIS' select agent programs have worked together to provide registered entities with additional guidance on the inventory requirements for working stocks and select agents that are held long term in storage. On February 12, 2009, CDC's and APHIS' select agent programs posted guidance on the definition of "long-term storage" as used in the Select Agent Regulations. This guidance is available on the National Select Agent Program's website at the following address: <http://www.selectagents.gov/complianceAssistance.htm>. Also, we will carefully review any recommendations regarding inventory control from the Working Group on Strengthening the Biosecurity of the United States and consider how to implement those recommendations.

The following are GAO's responses to the Department of Health and Human Service's (HHS) comments in a letter dated July 20, 2009.

GAO Comments

1. We agree with HHS. Our report acknowledges that no executive or legislative mandate currently requires any agency to gather this information and we are making a recommendation in this regard.
2. We agree that instituting new regulatory reporting requirements about the location of all BSL-3 laboratories could create a burden on private sector laboratories and would require new federal resources.
3. Our report did acknowledge information from CDC officials stating that at the time of both incidents, the new BSL-4 facility was not fully operational and that no agents were inside the facility. However, we believe that CDC is missing the point. Given that grounding cables were cut, it is apparent that the building's integrity as it related to adjacent construction was not adequately supervised. CDC officials stated that standard procedures under building codes did not require monitoring of the integrity of the new BSL-4 facility's electrical grounding. This incident highlighted the risks inherent in relying on standard building codes to ensure the safety of high-containment laboratories—as there are no building codes and testing procedures specifically for those laboratories. We agree with CDC that high-containment laboratories include a three-legged and multi-tiered approach to containment. However, to have a fully safe system of containment, any failure of one tier or one of the legs needs to be rapidly identified and corrected. Our focus in this incident was on CDC's power system and lessons that can be learned for other high-containment labs.
4. We modified the language in our report to note that a loss of power could have serious consequences under certain circumstances.
5. While we agree that critical differences, purposes, and functions differentiating code-required emergency power and legally required standby power are important when planning and designing electrical distribution systems for biological laboratories and other science buildings, this does not materially affect our findings.
6. We disagree with CDC that the titer should be at least four times higher than the baseline level to be considered an exposure. Most importantly, any increase in titers involving an agent that is being worked on at a laboratory should be taken seriously and investigated.

The laboratory safety aspect of antibody titers is clearly different from those that apply to a general clinical situation. The increase in titers may indicate natural exposure to the agent (depending on the agent and location of the lab) or result from inconsistencies associated with laboratory testing. Most serological assays for select agents are not commonly conducted in clinical laboratories and are primarily performed in research laboratories. As such, these assays may not be properly controlled and validated. Assay-to-assay variation may be high, especially if experience is limited. Additionally, such assays are not particularly robust unless baseline specimens are available for comparison testing and serum samples are collected within relatively short time frames (for example, 3 to 6 months).

7. We agree with HHS that national goals may change over time. Therefore, it is important that the strategic evaluation of high-containment laboratories be undertaken periodically. We have modified our recommendation to include periodic evaluation.
8. Our report recommends that a single entity be charged with governmentwide strategic evaluation of high-containment laboratories. While we agree that there are several challenges, having a single agency would facilitate a coordinated response.
9. We agree that future evaluations of laboratory capacity and supply should examine the needs of the clinical laboratories related to their high-containment capacity. However, knowing the number of laboratories is a key requirement to making such evaluation effective.
10. We disagree. We believe that national standards contribute to ensuring that all high-containment laboratories meet minimum standards. National standards are valuable not only in relation to new laboratory construction but also in ensuring compliance for periodic upgrades. We agree that BMBL provides guidance on design and construction; however, the guidance does not provide standards that must be adhered to. While sharing lessons learned can be beneficial to meeting standards, it is not an adequate substitute for the standards themselves. If existing laboratories do not meet national standards, we believe that these laboratories need to be brought into compliance.

Appendix VIII: Comments from the Department of Agriculture



United States Department of Agriculture

Office of the Secretary
Washington, D.C. 20250

AUG 19 2009

Dr. Sushil Sharma, Assistant Director
Applied Research and Methods
Center for Technology and Engineering
U.S. Government Accountability Office
441 G Street, NW
Washington, DC 20548

Dear Dr. Sharma:

The U.S. Department of Agriculture (USDA) appreciates the opportunity to review and provide comments on the GAO Draft Report, "High Containment Laboratories: Coordinated National Oversight Is Needed" (09-574). We have addressed the Recommendations for Executive Action that pertain to USDA.

GAO Recommendation

We recommend that the National Security Advisor, in consultation with the Secretaries of Health and Human Services, Agriculture, Defense, and Homeland Security; the National Intelligence Council; and other executive departments as deemed appropriate identify a single entity charged with governmentwide strategic evaluation of high-containment labs that will (1) determine the number, location, and mission of the labs needed to effectively meet national goals to counter biothreats; the existing capacity within the United States; the aggregate risks associated with the labs' expansion; and the type of oversight needed; and (2) develop, in consultation with the scientific community, national standards for the design, construction, commissioning, and operation of high-containment labs, specifically including provisions for long-term maintenance.

USDA Response

USDA agrees with this Recommendation, and will work with the National Security Advisor and other agencies to determine the appropriate body that should be charged with governmentwide strategic evaluation for high-containment labs. Further, USDA will also work cooperatively on establishing national standards for the design, construction, commissioning, and operation of high-containment laboratories.

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Dr. Sushil Sharma
Page 2

Two interdepartmental work groups have also reviewed issues related to oversight of high- and maximum-containment laboratories. The Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight (co-chaired by USDA and the Department of Health and Human Services (HHS)) focused its evaluation on Federal facilities, while the Biosecurity Working Group (formed in response to Executive Order 13486, "Strengthening Laboratory Biosecurity in the United States,") focused on security and personnel reliability for Federal, State, and private facilities. The Trans-Federal Task Force, and the Biosecurity Working Group will be submitting their recommendations to Congress and the White House on similar issues. The recommendations submitted from these evaluations may affect the scope of work discussed in these GAO recommendations.

GAO Recommendation

We recommend that the Secretaries of Health and Human Services and Agriculture develop (1) a clear definition of exposure to select agents and (2) a mechanism for sharing lessons learned from reported lab accidents so that best practices for other operators of high-containment labs can be identified.

USDA Response

USDA agrees with this Recommendation. However, USDA believes that the Federal Select Agent Program (i.e., HHS' Centers for Disease Control and Prevention's (CDC) Division of Select Agents and Toxins, and USDA's Animal and Plant Health Inspection Service's (APHIS) Agriculture Select Agent Program) has provided a sufficiently clear definition of occupational exposure: "any event which results in any persons in a registered entity, facility or lab not being appropriately protected in the presence of an agent or toxin. This may include reasonably anticipated skin, eye, mucous membrane, or parenteral contact with blood or other potential infectious materials that may result from the performance of a person's duties. For example, a sharps injury from a needle being used in select agent or toxin work would be considered an occupational exposure." This definition is derived from the Occupational Safety and Health Administration Bloodborne Pathogens Standard in title 29, *Code of Federal Regulations* (29 CFR), part 1910-1030b) and is jointly published in the "Select Agents and Toxins Theft, Loss and Release Information Document," dated January 18, 2008. The document is currently posted on the Federal Select Agent Web site.

USDA agrees with GAO that reported laboratory incidents can be summarized and published in a format that can help other entities learn from the incidents. USDA's APHIS will work with CDC to develop and complete an effective process, by December 2010.

Dr. Sushil Sharma
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GAO Recommendation

Should the Secretaries consider implementing a personnel reliability program for high-containment labs to deal with insider risk, we recommend that they evaluate and document the cost and impact of such a program.

USDA Response

USDA agrees with this Recommendation. Should the Secretary of USDA consider implementing a personnel reliability program as part of our regulatory responsibilities, we will evaluate and document the cost and impact of such a program. The Biosecurity Working Group will address the issue of implementing personnel reliability programs in high-containment laboratories, and will provide additional information and possible recommendations on personnel reliability programs to be implemented in registered facilities.

Further, USDA currently has a personnel reliability program for its own laboratories, as outlined in "USDA Departmental Manual 9610-001: USDA Security Policies and Procedures for Biosafety Level – 3 Facilities," which sets the policy on suitability requirements for USDA and non-USDA personnel requiring access to BSL-3 facilities. This document will soon be revised. However, as stated before, should USDA implement a new personnel reliability program, the agency will consider the cost and impact of such a program.

GAO Recommendation

Recognizing that biological agent inventories cannot be completely controlled at present, we also recommend that the Secretaries of Health and Human Services and Agriculture review existing inventory control systems and invest in and develop appropriate technologies to minimize the potential for insider misuse of biological agents.

USDA Response

USDA agrees with this Recommendation, and will review inventory control systems used by regulated laboratories and other laboratories working with pathogens. The Biosecurity Working Group has addressed inventory control systems in its review, and its report will probably include some recommendations on this issue. USDA and HHS will review existing inventory control systems within the context of the Federal Select Agent Program by December 2010 and will decide, by December 2011, whether to change existing regulations.

Pertinent to the issue of inventory control, the Federal Select Agent Program has developed a guidance document on long-term storage. This document, "Guidance on the Definition of Long Term Storage as Used in the Select Agent Regulations," is posted on the Federal Select Agent Program Web site. Based on comments from multiple public meetings, the document will be

**Appendix VIII: Comments from the
Department of Agriculture**

Dr. Sushil Sharma
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expanded to include more specific guidance on working stocks, inventory procedures, and examples of inventory systems. We will have this guidance updated by December 2010.

Sincerely,



Ann Wright
Deputy Under Secretary
Marketing and Regulatory Programs

Appendix IX: GAO Contact and Staff Acknowledgments

GAO Contact

Nancy Kingsbury, (202) 512-2700 or kingsburyn@gao.gov

Staff Acknowledgments

In addition to the contact named above, Sushil Sharma, Ph.D., DrPH (Assistant Director), Amy Bowser, George Depaoli, Terrell Dorn, Jeff McDermott, Jean McSween, Jack Melling, Ph.D., Corey Scherrer, Linda Sellevaag, and Elaine Vaurio made key contributions to this report.

Related GAO Products

Biological Research: Observations on DHS's Analyses Concerning Whether FMD Research Can Be Done as Safely on the Mainland as on Plum Island [GAO-09-747](#). Washington, D.C.: July 30, 2009.

Biosafety Laboratories: BSL-4 Laboratories Improved Perimeter Security Despite Limited Action by CDC. [GAO-09-851](#). Washington, D.C.: July 7, 2009.

Biosafety Laboratories: Perimeter Security Assessment of the Nation's Five BSL-4 Laboratories. [GAO-08-1092](#). Washington, D.C.: September 17, 2008.

High-Containment Biosafety Laboratories: DHS Lacks Evidence to Conclude that Foot-and-Mouth Disease Research Can be Done Safely on the U.S. Mainland. [GAO-08-821T](#). Washington, D.C.: May 22, 2008.

High-Containment Biosafety Laboratories: Preliminary Observations on the Oversight of the Proliferation of BSL-3 and BSL-4 Laboratories in the United States. [GAO-08-108T](#). Washington, D.C.: October 4, 2007.

Biological Research Laboratories: Issues Associated with the Expansion of Laboratories Funded by the National Institute of Allergy and Infectious Diseases. [GAO-07-333R](#). Washington, D.C.: February 22, 2007.

Homeland Security: Management and Coordination Problems Increase the Vulnerability of U.S. Agriculture to Foreign Pests and Disease. [GAO-06-644](#). Washington, D.C.: May 19, 2006.

Plum Island Animal Disease Center: DHS and USDA Are Successfully Coordinating Current Work, but Long-Term Plans Are Being Assessed. [GAO-06-132](#). Washington, D.C.: December 19, 2005.

Homeland Security: Much Is Being Done to Protect Agriculture from a Terrorist Attack, but Important Challenges Remain. [GAO-05-214](#). Washington, D.C.: March 8, 2005.

Combating Bioterrorism: Actions Needed to Improve Security at Plum Island Animal Disease Center. [GAO-03-847](#). Washington, D.C.: September 19, 2003.

Homeland Security: CDC's Oversight of the Select Agent Program. [GAO-03-315R](#). Washington, D.C.: November 22, 2002.

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United States Government Accountability Office
Washington, DC 20548

February 25, 2013

Congressional Requesters

Subject: *High-Containment Laboratories: Assessment of the Nation's Need Is Missing*

High-containment laboratories, biosafety level (BSL)-3 and BSL-4 laboratories, are used to (1) develop medical and veterinary countermeasures against biological agents and (2) research the risks these agents pose to human health, animal health, the food supply, and the U.S. economy. In 2009 we reported on the expansion of these laboratories, which began in the 1990s and accelerated after the 2001 anthrax attack.¹ We found that although this expansion was occurring, no single federal agency was responsible for assessing overall laboratory needs.² Instead, departments and agencies only assessed laboratory needs that were within the scope of their respective missions. We therefore determined that a national strategy for oversight, including periodic assessments of the nation's need for these laboratories, was called for. We also found that the absence of national standards for laboratory design, construction, commissioning, operations, and maintenance raised concerns and increased the risk of laboratory accidents.

Our 2009 report made two recommendations to the National Security Advisor, located in the Executive Office of the President (EOP), to address these weaknesses.³ Specifically, we recommended that the National Security Advisor identify a single entity, charged with periodic government-wide strategic evaluation of high-containment laboratories, that will (1) determine (a) the number, location, and mission of the laboratories needed to effectively meet national goals to counter biothreats; (b) the existing capacity within the United States; (c) the aggregate risks associated with the laboratories' expansion; and (d) the type of oversight needed and (2) develop, in consultation with the scientific community, national standards for the design, construction, commissioning, and operation of high-containment laboratories, specifically including provisions for long-term maintenance.

¹GAO, *High-Containment Laboratories: National Strategy for Oversight Is Needed*, [GAO-09-574](#) (Washington, D.C.: Sept. 21, 2009). High-containment laboratories include biosafety level (BSL)-3, animal biosafety level (ABSL)-3 laboratories, and BSL-4 laboratories that study agents that have the potential for respiratory transmission and that may cause serious and potentially lethal infections. See also the related GAO products section at the end of this report for a list of reports that represent the body of GAO work on high-containment laboratories.

²In 2009 we reported that there were over 240 entities with at least 1,362 BSL-3 laboratories in the United States registered with the Centers for Disease Control and Prevention (CDC) in the Department of Health and Human Services, and Animal and Plant Health Inspection Service in the Department of Agriculture, under the Federal Select Agent Program. In 2010, 1,495 laboratories were registered with the CDC as cited in Jocelyn Kaiser, "Taking Stock of the Biodefense Boom," *Science*, vol. 333, (Sept. 2, 2011). But this is only an incomplete estimate of the total number of all high-containment laboratories in the United States since there are an undetermined number of laboratories that do not work with select agents.

³The National Security Advisor is the head of the National Security Staff.

This report addresses the following questions:

1. What actions have been taken to implement the recommendations made in our 2009 report?
2. To what extent is action still needed concerning (1) an assessment of the nation's need for high-containment laboratories, including their numbers, functions, and research priorities and (2) the development of any national standards for designing, constructing, commissioning, maintaining, and operating high-containment laboratories?

To assess implementation of our 2009 report recommendations, we interviewed officials of the National Security Staff (NSS). We also reviewed documents for evidence of any current assessments of the nation's need, including research priorities and capacity for all high-containment laboratories, and evidence of national standards. To determine if action is still needed, we compared that evidence with the conditions GAO reported on in 2009: no assessment of national capacity to meet national goals and no national standards. The continued absence of such assessment and national standards would be reasons for further action. We interviewed officials in the Office of Science and Technology Policy (OSTP) in the EOP and reviewed documents they identified, as well as others we subsequently identified, including those from the National Academy of Sciences (see enc. I for a complete list of documents reviewed).

We conducted our work from February 2010 through December 2012 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

Actions Not Yet Taken to Implement GAO's 2009 Recommendations

In accordance with our normal procedures, we sought comments on a draft of our 2009 report, which included our recommendations to the National Security Advisor, from the EOP. However, the EOP did not provide comments on the draft of the report. Subsequent to the report's issuance, a designated representative of the NSS stated that "The NSS has considered the recommendations of the GAO regarding designating a single entity charged with periodic governmentwide strategic evaluation of high-containment laboratories and has determined that it is not in the best interests of U.S. national security to allocate resources in that way." The designated representative of the NSS also did not tell us of any action taken on the recommendations.⁴ Subsequently, we asked the NSS, among other things, what criteria the NSS used to determine that designating a single entity was not in the best interests of national security to allocate resources that way. The NSS did not further discuss

⁴We reviewed the President's National Security Strategy (2010); the National Strategy for Countering Biological Threats (November 2009), authored by the National Security Council; Executive Order 13546: Optimizing the Security of Biological Select Agents and Toxins in the United States (2010); and the President's Memorandum on Scientific Integrity (March 2009) and OSTP's subsequent guidance on it and found no evidence of such actions.

its decision making on this issue, but instead suggested that we direct any additional questions concerning high-containment laboratory oversight to the OSTP.

Accordingly, we contacted the OSTP to further discuss our recommendations.⁵ In October 2011 and September 2012, OSTP officials told us that while they did not agree with all parts of our recommendations, they were willing to engage us in discussions on how best, from their perspective, to address the 2009 report findings and implement our recommendations. The OSTP initially interpreted our first recommendation as creation of a single entity to conduct strategic evaluations, but we clarified that we were not specifying whether the entity would be conducting or coordinating periodic evaluations of, and the development of national standards for, high-containment laboratories. OSTP officials did not agree that a single entity should be charged with government-wide strategic evaluation of high-containment laboratories. Such an assessment was considered to be unnecessarily broad and cumbersome. However, they did support periodic, government-wide assessments of national biodefense research and development needs, including whether appropriate resources—including high-containment laboratories—meet those research and development needs. According to OSTP officials, they had taken some steps to examine the need for national standards for designing, constructing, commissioning, maintaining, and operating high-containment laboratories.

Full Assessment of Nation’s Need for High-Containment Laboratories and Standards Remains

Three years after our 2009 report, a comprehensive assessment of the nation’s need for high-containment laboratories, including research priorities and capacity, is still unavailable. In particular, no national entity or working group has published an assessment of the nation’s need that cuts across all agencies, universities, and the private sector. Further, there still are no national standards for designing, constructing, commissioning, and operating high-containment laboratories, including provisions for long-term maintenance.

The Nation’s Need for High-Containment Laboratories Is Still Unknown

There is still no one agency or group that knows the nation’s need for all U.S. high-containment laboratories, including the research priorities and the capacity, number and location, to address priorities. This deficiency may be more critical today than 3 years ago because current budget constraints make prioritization essential. Since the publication of our report in 2009, the number of high-containment laboratories has increased. Although modern high-containment technologies (for example, high-efficiency particulate air [HEPA] filtration) in conjunction with laboratory design have been effective in reducing the level of risk, there is nevertheless some degree of risk associated with design, construction, operations, and maintenance of high-containment laboratories. This was realized following a Centers for Disease Control and Prevention (CDC) power failure incident in Atlanta, Georgia, where no biological agent was released but that showed the difficulties in maintaining biological containment, and a leaky pipe incident in Pirbright, United Kingdom,

⁵Specifically, the OSTP mission is to help coordinate science and technology policy across the government; build partnerships among federal, state, and local governments and the private sector; and develop policies related to science and technology activity. OSTP also coordinates governmentwide policy regarding the biosafety, biosecurity, and biocontainment of high-containment laboratories.

that failed to maintain biological containment.⁶ Increasing the number of laboratories also increases the aggregate national risk.

In addition, the current budget constraints may already have affected our national capacity to address certain research priorities. For example, according to a 2012 National Academy of Sciences report, a critical need exists for giving priority to a modern animal biosafety level-4 (ABSL-4) laboratory with large-animal capacity.⁷ Such a laboratory would be able to safely research, develop, and test vaccines for catastrophic foreign animal diseases, such as foot-and-mouth disease, and high-risk zoonotic diseases with the potential to severely harm human health. The Department of Homeland Security had stated that its proposed new National Bio- and Agro-Defense Facility laboratory, estimated to cost \$1.14 billion to construct, would address that research priority. However, faced with the nation's current budget constraints, achieving that research priority could be in doubt.

No National Standards for Designing, Constructing, Commissioning, Operating, and Maintaining High-Containment Laboratories

We found a continued lack of national standards for the design, construction, commissioning, and operation of high-containment laboratories. These laboratories are expensive to build, operate, and maintain. As we noted in our 2009 report, in the absence of national standards, it is likely that there may be variations resulting from local requirements, but without an underpinning set of standards to ensure safe operations. In the absence of some fundamental criteria, each laboratory can be designed, constructed, and maintained according to local requirements. This will make it difficult to be able to assess and guarantee safety, as we noted in our 2009 report. For example, while investigating a power outage incident in its recently constructed BSL-4 laboratory, the CDC later determined that, some time earlier, a critical grounding cable buried in the ground outside the building had been cut by construction workers digging at an adjacent site. The cutting of the grounding cable, which had hitherto gone unnoticed by CDC facility managers, compromised the electrical system of the facility that housed the BSL-4 laboratory. Given that grounding cables were cut, it is apparent that the building's integrity as it related to adjacent construction was not adequately supervised. CDC officials stated in 2009 that standard procedures under local building codes did not require monitoring of the integrity of the new BSL-4 facility's electrical grounding. This incident highlighted the risks inherent in relying on local building codes to ensure the safety of high-containment laboratories, as there are no building codes and testing procedures specifically for those laboratories.

The Biosafety in Microbiological and Biomedical Laboratories document, often referred to as the BMBL, provides guidance on design, construction, and operations; however, that guidance does not equate to standards that should be adhered to or ways to determine if such standards have been achieved.⁸ National standards are valuable not only in relation to

⁶See [GAO-09-574](#) for more information on this incident.

⁷National Research Council, Committee on an Analysis of the Requirements and Alternatives for Foreign Animal and Zoonotic Disease Research and Diagnostic Laboratory Capabilities, *Meeting Critical Laboratory Needs for Animal Agriculture: Examination of Three Options* (Washington, D.C.: National Academies Press, 2012).

⁸Department of Health and Human Services, *Biosafety in Microbiological and Biomedical Laboratories*, 5th ed. (Atlanta, Ga.: December 2009, <http://www.cdc.gov/biosafety/publications/bmbl5> (accessed Feb. 19, 2013).

new laboratory construction but also for periodic upgrades. Therefore, national standards would contribute to ensuring that all high-containment laboratories meet minimum acceptable standards. Such standards need not be a constraining “one-size fits all” model, but can inform as to levels of performance to be achieved.

Conclusion

As we demonstrated in our 2009 report, assessment of the nation’s need for high-containment laboratories, including research priorities and capacity, is essential. The absence of such an assessment hampers planning for existing and future research priorities and capacity of high-containment laboratories. The OSTP is in a position to assess this need, as well as determine whether and where overlap and gaps exist.⁹ OSTP officials are also in a position to coordinate agency efforts, directly or through the efforts of working groups, across the government.

In addition, the cost of building and maintaining high-containment laboratories, combined with the current lack of national standards and the uncertainty about the number of high-containment laboratories needed to address priorities, exposes the nation to risk.

Therefore, the recommendations in our 2009 report are still valid. Modern high-containment technologies have been effective in reducing the level of risk. Nevertheless with the absence of national standards for design, construction, operation, and maintenance of high-containment laboratories, risk remains. Increasing the number of laboratories necessarily increases the aggregate national risk. In view of the inaction to date by the National Security Advisor on our previous recommendations and the potential for the OSTP to take action in its place, we are redirecting our recommendations to the OSTP.

Recommendations for Executive Action

We recommend that the OSTP ensure that periodic assessments of national biodefense research and development needs are conducted. These assessments would include whether appropriate resources, in particular, high containment laboratories, exist to meet those needs. We also recommend that the OSTP examine the need to establish national standards relating to designing, constructing, commissioning, maintaining, and operating high-containment laboratories.

Agency Comments and Our Evaluations

We obtained written comments on a draft of our report from the EOP’s OSTP, which are reprinted in enclosure II. OSTP concurred with our recommendations.

OSTP also stated that biodefense research, development, testing and evaluation are crucial to the long-term health and wellness of our population, animals, plants, the environment, and our economy. We agree. In its agency letter OSTP noted four separate actions taken by this administration in support of these efforts, see enclosure II. These actions focus on the

⁹GAO has reported on overlap and duplication in various programs. GAO, *2012 Annual Report: Opportunities to Reduce Duplication, Overlap and Fragmentation, Achieve Savings, and Enhance Revenue*, [GAO-12-342SP](#), (Washington, D.C.:Feb. 28, 2012).

work conducted in high-containment laboratories and the agents worked with in these laboratories as opposed to the laboratories themselves. OSTP officials also provided technical comments, which have been addressed in the body of our report as appropriate.

There are two areas in which OSTP disagreed with GAO in its technical comments.

First, OSTP disagreed that there has been an expansion of high-containment laboratories. As there is no reliable source of the total number of high-containment laboratories in the United States, we used the number of high-containment laboratories registered with one federal program, the Federal Select Agent Program, to estimate the number of all high-containment laboratories (see footnote 2). The number of registered high-containment laboratories (BSL-3 and BSL-4) has increased from 1,362 in 2008 to 1,495 in 2010.¹⁰ Even this estimate is an incomplete picture of all the high-containment laboratories, but it is based on the most-credible source.

Second, OSTP also disagreed with our assessment of the increased overall risk associated with the expansion of high-containment laboratories. Officials did not agree that there was an increased risk. Our assessment is based on probability theory, and we make no assumptions about the magnitude (size or extent) of the increase. The risk associated with any single laboratory is non-zero, for example, as laboratory accidents happen. Even where the newer safety controls reduce the risk of an accident for any individual laboratory, and even if the number of accidents at any laboratory is small, when the number of units (laboratories) increases, each laboratory's risk adds to the overall risk of an accident happening nationwide. As laboratories operate independently, the risk is not increased for each laboratory. The risk at each laboratory leads to an overall increased risk with expansion.

As agreed with your office, unless you publically announce the contents of this report earlier, we plan no further distribution until 30 days from the report date. At that time, we will send copies of this report to the Executive Office of the President (EOP) and other interested parties. In addition, this report is available at no charge on the GAO website at <http://www.gao.gov>.

If you or your staff has any questions about this report, please contact me at (202) 512-2700 or kingsburyn@gao.gov. Key contributors to this report were Sushil Sharma, Ph.D., Dr.PH, Assistant Director; Amy Bowser, Penny Pickett, Laurel Rabin, and Elaine Vaurio.



Nancy Kingsbury, Ph.D.
Managing Director
Applied Research and Methods

¹⁰In 2004 the number of laboratories registered with that program was 415, as we noted in GAO-09-574.

List of Requesters

The Honorable Fred Upton
Chairman
The Honorable Henry Waxman
Ranking Member
Committee on Energy and Commerce
House of Representatives

The Honorable Tim Murphy
Chairman
Subcommittee on Oversight and Investigations
Committee on Energy and Commerce
House of Representatives

The Honorable Joe Barton
House of Representatives

The Honorable Michael Burgess
House of Representatives

The Honorable Greg Walden
House of Representatives

Enclosure I: Documents Reviewed to Identify Actions on GAO's 2009 Recommendations

This is a list of documents we reviewed for evidence of (1) a current assessment of the nation's need, including research priorities and capacity, for all high-containment laboratories and (2) national standards on designing, constructing, commissioning, operating, and maintaining high-containment laboratories.

Centers for Disease Control and Prevention and Association of Public Health Laboratories. "Guidelines for Biosafety Laboratory Competency," *Morbidity and Mortality Weekly Report*. suppl., vol. 60 (April 15, 2011).

Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories*, 5th ed. Atlanta, Georgia: December 2009. HHS pub. no. (CDC) 21-1112. <http://www.cdc.gov/biosafety/publications/bmb15> (accessed Feb. 19, 2013).

Executive Order No. 13546, 75 Fed. Reg. 39,439 (July 8, 2012). Optimizing the Security of Biological Select Agents and Toxins in the United States (July 8, 2012).

National Academy of Sciences and National Research Council, Committee on Anticipating Biosecurity Challenges of the Global Expansion of High-Containment Laboratories. *Biosecurity Challenges of the Global Expansion of High-Containment Laboratories*. Washington, D.C.: National Academies Press, 2012.

National Institutes of Health. *NIH Guidelines for Research Involving Recombinant DNA Molecules*, Washington, D.C.: October 2011.

National Research Council. Committee on an Analysis of the Requirements and Alternatives for Foreign Animal and Zoonotic Disease Research and Diagnostic Laboratory Capabilities. *Meeting Critical Laboratory Needs for Animal Agriculture: Examination of Three Options*, Washington, D.C.: National Academies Press, 2012.

S3: *Science, Safety, and Security*. www.phe.gov/S3. The Office of Science and Technology Policy's (OSTP) description of the website: "The U.S. Government has developed a new website entitled, S3: Science, Safety, and Security to address biosafety, biosecurity, biocontainment, and biorisk management. The goal of the website is to promote transparency and broader awareness about the evolving nature of biological agents that can be hazardous, and how to handle and use these agents safely and securely. This S3 website will allow the U.S. Government to share policies and best practices relating to biological risk management. The resources provided on the website include information for laboratory personnel who work with potentially hazardous biological agents, their supervisors, the management personnel of the institutions in which they work, policymakers, and the public. The S3 website will be updated and expanded to include more U.S. Government resources and information."

Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight. *Report of the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight*. Washington, D.C.: July 2009. <http://www.phe.gov/preparedness/legal/boards/biosafetytaskforce/Pages/default.aspx>. (Accessed Feb. 19, 2013).

Enclosure II: Comments from the OSTP

EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF SCIENCE AND TECHNOLOGY POLICY
WASHINGTON, D.C. 20502

January 25, 2013

Dr. Nancy Kingsbury
Managing Director, Applied Research and Methods
U.S. Government Accountability Office
441 G Street, NW
Washington, DC 20548

Dear Dr. Kingsbury:

Thank you for the opportunity to review and comment on the GAO's draft report, "High-Containment Laboratories: Assessing the Nation's Need" (GAO-13-466R).

We agree with the final recommendations in the draft report as crafted. However, we did find some errors in the text of the draft, which we have addressed in the enclosed technical report.

Biodefense research, development, testing, and evaluation are crucial to the long term health and wellness of our population, animals, plants, the environment, and our economy. The Administration is proud of the actions it has taken in support of these important endeavors, including:

- In November, 2009, the National Security Council published the *National Strategy for Countering Biological Threats*, which articulates priorities for domestic and international efforts to counter biological threats. Implementation of this Strategy across the Federal government has strengthened our ability to counter biological threats while reducing duplication across government programs.
- In July, 2010, the Administration released Executive Order (E.O.) 13546, *Optimizing Security of Biological Select Agents and Toxins in the United States*, which led to the publication of new Select Agent Regulations in October, 2012¹ that articulate requirements for improved security measures for laboratories and personnel handling biological agents and toxins that pose the greatest health risk to plants, animals, and humans.
- In July, 2011, the National Science and Technology Council Committee on Homeland and National Security chartered the Subcommittee on Biological Defense Research and Development (BDRD), to coordinate and collaborate on defensive research, development, testing, and evaluation addressing biological threats to national security.
- In May, 2012, the BDRD chartered an Interagency Biorisk Management Working Group to coordinate mechanisms for strengthening research laboratory biorisk management (biosafety, biocontainment, and biosecurity) and for promoting outreach and education programs that inform scientists, biosafety professionals, and the public on biorisk management.

1

<http://www.selectagents.gov/resources/CDC%20Select%20Agent%20Biennial%20Review%20Final%20Rule%2010%2005%202012.pdf>

We look forward to continuing our efforts in this domain and working with you in the future.

Sincerely,

A handwritten signature in cursive script that reads "Patricia Falcone".

Patricia Falcone, PhD
Associate Director for National Security and
International Affairs

Enclosure

Related GAO Products

Homeland Security: Actions Needed to Improve Response to Potential Terrorist Attacks and Natural Disasters Affecting Food and Agriculture. [GAO-11-652](#). Washington, D.C.: August 19, 2011.

Biological Laboratories: Design and Implementation Considerations for Safety Reporting Systems. [GAO-10-850](#). Washington, D.C.: September 10, 2010.

High-Containment Laboratories: National Strategy for Oversight Is Needed. [GAO-09-1045T](#). Washington, D.C.: September 22, 2009.

High-Containment Laboratories: National Strategy for Oversight Is Needed. [GAO-09-1036T](#). Washington, D.C.: September 22, 2009.

High-Containment Laboratories: National Strategy for Oversight Is Needed. [GAO-09-574](#). Washington, D.C.: September 21, 2009.

Biological Research: Observations on DHS's Analyses Concerning Whether FMD Research Can Be Done as Safely on the Mainland as on Plum Island. [GAO-09-747](#). Washington, D.C.: July 30, 2009.

Biosafety Laboratories: BSL-4 Laboratories Improved Perimeter Security Despite Limited Action by CDC. [GAO-09-851](#). Washington, D.C.: July 7, 2009.

Plum Island Animal Disease Center: DHS Has Made Significant Progress Implementing Security Recommendations, but Several Recommendations Remain Open. [GAO-08-306R](#). Washington, D.C.: December 17, 2007.

Biosafety Laboratories: Perimeter Security Assessment of the Nation's Five BSL-4 Laboratories. [GAO-08-1092](#). Washington, D.C.: September 17, 2008.

High-Containment Biosafety Laboratories: DHS Lacks Evidence to Conclude That Foot-and-Mouth Disease Research Can Be Done Safely on the U.S. Mainland. [GAO-08-821T](#). Washington, D.C.: May 22, 2008.

High-Containment Biosafety Laboratories: Preliminary Observations on the Oversight of the Proliferation of BSL-3 and BSL-4 Laboratories in the United States. [GAO-08-108T](#). Washington, D.C.: October 4, 2007.

Biological Research Laboratories: Issues Associated with the Expansion of Laboratories Funded by the National Institute of Allergy and Infectious Diseases. [GAO-07-333R](#). Washington, D.C.: February 22, 2007.

Homeland Security: Management and Coordination Problems Increase the Vulnerability of U.S. Agriculture to Foreign Pests and Disease. [GAO-06-644](#). Washington, D.C.: May 19, 2006.

Plum Island Animal Disease Center: DHS and USDA Are Successfully Coordinating Current Work, but Long-Term Plans Are Being Assessed. [GAO-06-132](#). Washington, D.C.: December 19, 2005.

Homeland Security: Much Is Being Done to Protect Agriculture from a Terrorist Attack, but Important Challenges Remain. [GAO-05-214](#). Washington, D.C.: March 8, 2005.

Combating Bioterrorism: Actions Needed to Improve Security at Plum Island Animal Disease Center. [GAO-03-847](#). Washington, D.C.: September 19, 2003.

Homeland Security: CDC's Oversight of the Select Agent Program. [GAO-03-315R](#). Washington, D.C.: November 22, 2002.

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CDC Lab Power Loss Raises Biosafety Concerns

GSN-NTI

July 20, 2007

Containment systems for deadly germs shut down last month at a leading U.S. bioterrorism defense lab, underscoring security doubts within the biological research industry, the Atlanta Journal-Constitution reported today (see GSN, July 5).

Generators running germ-trapping air pumps were knocked out for an hour during a lightning storm, potentially jeopardizing the safety cordon around sensitive research areas at the facility in DeKalb County, Georgia.

"I don't think there is anything we'll ever be able to do to totally prevent power outages at CDC," said spokesman Tom Skinner of the Centers for Disease Control and Prevention, which operates the laboratory. "What we have to do is move toward minimizing the duration of the time we are without power."

While the venting system went down, scientists were able to safely secure their experiments using 15 to 20 minutes of reserve battery power, said laboratory architect Jon Crane.

The site contains facilities that have worked on avian influenza, anthrax and the 1918 pandemic flu virus, though it is not known what experiments were under way when the lightning struck.

A biosafety expert called for closure of the research facility until the power loss is fully explained and addressed, the Journal-Constitution reported.

"This is an astonishing design lapse," said molecular biologist Richard Ebright of Rutgers University.

"It's just remarkable that a building of such national prominence, intended for work with some of the most lethal agents, was designed and constructed without an effective backup power system."

The CDC laboratories have reinforced containment systems that protect workers and the public in power outages, the agency and other experts said. Potentially contaminated air did not leak outward when the pumps went down, said Casey Chosewood, CDC health and safety officer.

Ebright said he worried about the laboratory workers who depend on constant air ventilation.

"In those cases, there could be potential exposure of the individuals carrying out the experiments," he said.

At the DeKalb County facility, more than just safety systems rely on a constant power supply, said security expert Jeanne Guillemain of the Massachusetts Institute of Technology.

"All your security that's relying on power just went down. It's not good," she added (Alison Young, Atlanta Journal-Constitution, July 20).

CDC action at germ lab questioned

Duct tape used to seal door inside Atlanta facility after possible leak of bioterror bacteria last year.

By Alison Young

The Atlanta Journal-Constitution

Published on: 06/22/08

At the Centers for Disease Control and Prevention's new \$214 million infectious disease laboratory in Atlanta scientists are conducting experiments on bioterror bacteria in a room with a containment door sealed with duct tape.

The tape was applied around the edges of the door a year ago after the building's ventilation system malfunctioned and pulled potentially contaminated air out of the lab and into a "clean" hallway.

Nine CDC workers were tested in May 2007 for potential exposure to the Q fever bacteria being studied in the lab, CDC officials said this week in response to questions from The Atlanta Journal-Constitution.

The air-flow incident occurred very early in the morning, before the workday began. The blood tests were done out of an "abundance of caution," CDC spokesman Tom Skinner said, and they showed that none of the workers who arrived after the incident were infected.

Q fever, which causes high fevers and sometimes fatal heart problems, is most commonly spread when humans inhale bacteria-laden dust from contaminated animal waste. Human-to-human transmission is rare. It is classified as a potential bioterror agent because it is moderately easy to disseminate.

The CDC Q fever lab's air containment systems have since worked properly, agency officials said; the lab is safe and poses no risk to workers. The public was never at any risk because numerous security layers were in place between the lab and the outdoors, they said.

Yet the duct tape remains in place.

"It's an enhancement," said Patrick Stockton, CDC safety and occupational health manager, as he and four other agency officials took a reporter to see the door Wednesday. "We could take it off."

Critics want answers

The CDC's explanations drew skepticism from some biosafety watchdogs — especially since this is the same lab building that came under scrutiny by Congress and the Government Accountability Office last summer after the AJC revealed the building experienced an hour-long power outage and backup generators failed to come on.

"I do not believe the CDC would approve this arrangement in a laboratory other than their own," Richard Ebright, a microbiologist and biosafety expert at Rutgers University in New Jersey, said of the taped Q fever lab door.

The CDC is the federal agency responsible for inspecting U.S. labs — including its own — that work with certain dangerous germs that primarily infect humans. Because the Q fever bacteria, *Coxiella burnetii*, can cause disease both in humans and animals, the U.S. Department of Agriculture has secondary inspection authority.

Despite accompanying CDC inspectors on evaluations of the Atlanta lab building housing the duct-taped Q fever door, USDA spokeswoman Rachel Iadicicco said that agency's inspectors were not aware of the use of duct tape. "We will discuss this with CDC," she said.

Ebright said duct-taping a door adjacent to Q fever experiments with mice "raises very serious concerns about management. And those concerns are particularly important when one bears in mind this facility will ultimately be handling a full range of lethal pathogens — up to and including smallpox."

The GAO, the investigative arm of Congress, has warned of the importance of door seals in two recent reports on the safety of the nation's high-containment laboratories.

"Because they are intended to contain dangerous microorganisms, usually in liquid or aerosol form, even minor structural defects — such as cracks in the wall, leaky pipes, or improper sealing around doors — can have severe consequences," said Nancy Kingsbury, the GAO's managing director of applied research and methods, in written testimony to Congress last month.

Ebright notes that the CDC's biosafety standards manual states: "Seams, if present, must be sealed." And duct tape wouldn't appear to be adequate, he said.

CDC officials said the Q fever lab is in full compliance with all rules. They said the CDC's lab inspectors are fully aware of the duct tape. "The lab is safe, and it's passed its inspections. But we want to make the lab even more safe and are doing so," said Skinner.

On Monday, designs were completed for a new self-sealing door to replace the one currently sealed with duct tape, said Ken Bowen, director of the CDC's Facilities Maintenance and Engineering Office. Even though it's not required, he said,

the new door is being added “as a precaution.”

The construction to install the new door will begin sometime between November and next April, possibly sooner, depending on when there is a good stopping point in the experiments being conducted by the Q fever scientists.

Concern in Congress

The duct tape and the air-handling incident add to concerns about the CDC’s new lab building, said Rep. John Dingell (D-Mich.), chairman of the House Committee on Energy and Commerce. His committee and the GAO have been investigating whether the post-Sept. 11 proliferation of public and private bioterrorism labs poses public safety risks.

“This is yet another incident that calls into question the CDC’s self-inspection policy. I highly doubt that the CDC would accept duct-taped doors on the privately owned bio labs it inspects,” Dingell said Friday.

“If the going rate for a leaky door and roll of duct tape is \$200 million, then I think I’m in the wrong line of business,” Dingell said.

Key labs not certified

The 368,000-square-foot lab building, known at the agency as Building 18, is formally called the Emerging Infectious Diseases Laboratory. It’s located on CDC’s main campus off Clifton Road.

Construction was completed in the fall of 2005 and about 500 workers and scientists moved into its many offices and labs. But the building’s crown jewel — a suite of four maximum containment Biosafety Level 4 labs — still hasn’t been certified as safe to operate nearly three years after it were supposed to open. These BSL-4 labs are designed to contain smallpox, Ebola and other lethal germs while scientists work in spacesuit-like protective gear.

CDC officials have said the delay is not a result of any major construction or design problems with the BSL-4 labs or the building. Rather, they said the agency’s earlier opening dates were unrealistic given the complexity and uniqueness of the new labs.

A year ago, The Atlanta Journal-Constitution requested under the Freedom of Information Act that the CDC release records about safety issues at the lab building, including last June’s power outage. So far the agency has not released any records.

On Dec. 18, the building was evacuated after its new medical waste incinerator was started for a test, then vented smoke into the high-containment lab area, according to internal CDC memos recently obtained by the AJC. Excessive heat caused the failure of the incinerator’s bypass stack, which tore away from its anchor bolts and fire caulk, the records show.

The damaged stack was repaired in January — under warranty and without additional taxpayer cost, CDC officials said last week. The incinerator problem has played no role in the delays, they said, and it has since been certified by state regulators and is now operational.

Air went the wrong way

The duct-taped Q fever lab, which is a Biosafety Level 3 (BSL-3) lab, is currently the only operating lab in the building’s “high-containment block,” which houses the four BSL-4 labs as well as three other BSL-3 labs.

One of the safety features of these high-containment labs is that they are designed to operate under negative air pressure, which keeps germs in by having air flow only in one direction. Air is constantly drawn from clean areas and halls into the lab, then vented outdoors through specially designed HEPA filters.

The incident that led to CDC lab workers having their blood tested began around 3 or 4 a.m. on May 25, 2007. That’s when CDC facilities staff shut down the building’s air handling system for maintenance, said Bowen. After the system was restarted, the Q fever lab lost its negative air pressure.

When workers arrived to begin their day, they discovered air coming out of the Q fever lab, rather than going into it, CDC officials said. “It pulled air out of that lab and into that corridor,” Bowen said.

A mix-up on doors?

The Q fever lab is somewhat unusual in its design, CDC officials acknowledge. To allow safe viewing of scientists’ work with Q fever bacteria and infected mice from a “clean” hallway, there typically would be a sealed glass window. But the lab has a door next to the window. Although it is locked and not used, it has no special seals along its edges, and allows the flow of air when not sealed with duct tape.

Seals are not required on BSL-3 lab doors, the CDC emphasized. The door was put there to increase the flexibility of the lab space, enabling it to someday be used for lower-level experiments that don’t require stringent BSL-3 precautions.

After the May 2007 incident when air was drawn out of the lab, the agency applied duct tape around all of the door’s edges as an added safeguard to control airflow.

Bowen and other CDC officials said there have been no other incidents where potentially contaminated air has blown out of the Q fever lab because air pressure changed from negative to positive.

But an inspection report written by a CDC animal lab consultant in March 2007, states: “Bldg. 18 — positive airflow from the Q fever laboratory into the clean hallway ... The door into the corridor was taped temporarily and did not adequately contain the airflow into this corridor. This issue must be corrected immediately to ensure the health and safety of personnel and research chimpanzees.”

The consultant, Bradford Goodwin Jr., declined to be interviewed. Goodwin, a veterinarian, is executive director of the Center for Laboratory Animal Medicine and Care at the University of Texas Health Science Center in Houston.

CDC officials said the duct-taped door that Goodwin cited in his report is a different door from the one that currently has tape on it. They said there was no positive air-flow problem — where air moved out of the lab — in March 2007.

“He misunderstood the fact that the door separated two clean corridors and therefore that resulted in misinformation being included in the report,” said Skinner, the CDC spokesman. Skinner noted the Q fever lab didn’t go “hot” and begin conducting experiments until two months after Goodwin’s visit.

But CDC officials agree that duct tape was on the door mentioned in Goodwin’s report. “This door was duct-taped as a means to stop entry and exit until an appropriate lock could be installed and to limit air transfers between the two clean corridors,” CDC officials said in a written statement.

Some experts said it’s difficult to gauge the significance of the duct tape on the lab doors without more information.

“It could be inconsequential or it could be consequential,” said Chris Newcomer, executive director of the Association for Assessment and Accreditation of Laboratory Animal Care International, commenting in general and not about CDC’s lab in particular.

“There’s nothing intrinsically dangerous about duct tape or repair with duct tape on the seal of a door,” Newcomer said.

WHAT IS Q FEVER?

Q fever is a disease caused by the bacteria *Coxiella burnetii*. It primarily affects cattle, sheep and goats. But humans are very susceptible to the disease, usually through inhaling airborne bacteria. Only a few organisms are needed to cause infection. Human-to-human transmission is rare.

MORE ON Q FEVER

Only about half the people infected with Q fever will show signs of illness, such as high fevers that last a week or two, severe headaches, confusion, nausea, pneumonia and chest pain. Only about 1 percent to 2 percent of people with acute Q fever die from it. In rare cases, people suffer chronic Q fever infections that damage their hearts, and as many as 65 percent of those will die from the disease.

In 2006, three researchers at Texas A&M University were infected with Q fever. The exposures at Texas A&M’s lab, along with other mishaps, led to CDC inspectors last summer suspending the university’s authorization to work with certain bioterror agents.

The CDC took the action after a now-defunct biodefense watchdog group, the Sunshine Project, obtained and published documents about incidents inside the university’s labs. The university has agreed to pay a \$1 million fine for safety lapses.

Source: Centers for Disease Control and Prevention; AJC research

Airflow problems plague CDC bioterror lab
By Alison Young, USA TODAY
6/12/2012

A \$214 million bioterror germ lab at the Centers for Disease Control and Prevention in Atlanta has had repeated problems with airflow systems designed to help prevent the release of infectious agents, government documents and internal e-mails show.

While the agency says no one has been infected, a biosafety expert says the problems appear to be major violations of laboratory operating standards.

The area of the building with problems involves Biosafety Level 3 labs that can be used for experiments involving anthrax, dangerous strains of influenza, the SARS coronavirus, monkeypox and other microbes that have the potential to be used as bioweapons.

In February, air from inside a potentially contaminated lab briefly blew outward into a "clean" corridor where a group of visitors weren't wearing any protective gear which raised concern about exposure risks, according to e-mails reporting and discussing what happened. Research animals in the lab had not yet been infected at the time of the incident, the records say.

CDC engineers have raised written concerns about the air containment systems since at least 2010. At that time, scientists working with poxviruses, such as monkeypox, expressed concerns about airflow and said they "don't want to go into that facility because they don't feel comfortable with the way it is currently designed," according to minutes from a February 2010 meeting to discuss reversing the way air flowed through the labs and animal-holding areas.

According to the minutes, CDC safety manager William Howard said: "Bottom line is we can't continue to operate the building the way it is ... if (a bioterror lab inspector) finds out air is moving this direction they will shut this place down."

The CDC refused to grant interviews or answer any questions submitted in writing about the problems inside the high-containment labs and animal-holding area of the agency's 11-story Emerging Infectious Diseases Laboratory, also known as CDC Building 18.

In a statement, the CDC said there have been no releases of germs and no one has been injured.

Experiments in the building's high-containment labs are "done in an environment with highly skilled staff, technical equipment, and safety systems that unfortunately, at times, experience challenges. Fortunately, this unique facility has multiple systems in place that provide appropriate redundancy, so when there is an incident, the public's safety, as well as worker safety, is not compromised." The agency said it always takes "appropriate steps" to address incidents when they occur, but provided no details.

BSL-3 labs are required under federal safety guidelines to have "sustained directional airflow by drawing air into the laboratory from 'clean' areas toward 'potentially contaminated' areas."

The airflow system is designed to protect against the release of microbes, especially those that have the potential to become airborne and infect workers who could spread disease in the community.

The CDC is responsible for inspecting its own labs, as part of a federal program where it also oversees labs nationwide that work with germs or toxins that could potentially be used as bioweapons.

Rutgers University biosafety expert Richard Ebright said excerpts of CDC documents provided to him by USA TODAY "raise serious concerns. There appear to be significant irregularities." The problems seem to be the type that CDC's inspectors "would flag as major violations in inspections of non-CDC facilities," Ebright said.

The same lab building, which opened in 2005 and was touted by the agency as the world's most advanced laboratory, made news in 2007 when backup generators didn't work to keep airflow systems working during a power outage, then again in 2008 for a high-containment lab door that was being sealed with duct tape. The duct tape was applied after a 2007 incident where a ventilation system malfunctioned and pulled potentially contaminated air out of the lab and into a "clean" hallway; nine CDC workers were tested for potential exposure to Q fever bacteria. None were infected.

Most CDC staff quoted in the documents obtained by USA TODAY referred questions to the agency's press office or did not respond to requests for interviews.

Anthony Sanchez, the building's high-containment lab manager, in a brief interview said that although no building is perfect, "the scientists are happy with the facility ... It is safe, and we have highly professional persons working in there, and they don't have anything to worry about." Sanchez added: "I think the American public has gotten its money worth, and more."

The records show that other CDC staff have expressed safety concerns.

The CDC "will do anything ... to hide the fact that we have serious problems with the airflow and containment in this whole building," wrote CDC animal resources biologist Kismet Scarborough in an April 9 e-mail to several agency officials, including CDC Director Thomas Frieden. Scarborough's CDC voice-mail greeting describes her position as a high-containment lab manager for the agency's Animal Resources Branch.

Scarborough, e-mails indicate, was a witness to the Feb. 16 incident. where air blew out of a potentially contaminated BSL-3 lab into a "clean" corridor.

Another witness was Eddie Jackson, a biologist and inspector with CDC's Division of Select Agents and Toxins - the arm of CDC that is responsible for inspecting U.S. labs that work with bioterror germs.

Jackson e-mailed a top CDC safety official the day the incident happened. Jackson described how he was part of an escorted group standing outside the door of a lab when an animal technician inside opened an interior door to an animal room. "As the door closed a very noticeable puff of air could be felt coming through the slit in the window out into the 'clean' corridor."

Jackson noted in his e-mail that Scarborough told him the room didn't house infected animals at the moment, but there is a room with infected animals on the same corridor. He asked whether there is any risk of exposure for people walking down the hallway without respiratory protection. "Don't know whether this was a fluke or the norm, and the reason I'm commenting is one of the visitors seemed concerned and has been talking about it since we've come back," Jackson wrote.

It is unknown what answer Jackson received to his question. According to Scarborough's April 9 e-mail, CDC safety officials dismissed concerns about the incident saying "it doesn't matter if the dirty BSL 3 lab blows positive into the clean corridor as long as it is not sustained." Scarborough called this a "totally ridiculous response" and wrote that she is "horrified and dismayed at the events surrounding safety and the fact that even though this has been taken care of the chain of command all the way to Dr. Frieden, no one is willing to admit the mistake or more importantly fix it."

The mistake Scarborough appears to reference is a decision CDC implemented around late 2010 to re-engineer the air movement within these labs and nearby animal-holding areas. CDC engineers warned in early 2010 that reversing the airflow in this area could have "unintended consequences," including back-washing dirty air into clean areas when doors are opened and closed.

According to presentation slides for a February 2010 meeting about reversing the airflow in the lab and animal areas, CDC engineers Karen Moss and Tom Blanchard wrote that with the proposed changes "the potential exists to create large airflow disturbances, vortices and flow mixing between corridor and rooms will result, rooms may become same pressure as dirty corridor." If the airflow is going to be reversed, they wrote, anterooms - with negative air pressure - would need to be built to preserve airflow integrity. The records indicate that CDC never built the anterooms, in part because of concerns about cost and time delays, and because some safety officials questioned whether they were necessary.

In a February 2010 e-mail, Blanchard proposed sending a bluntly worded memo to the agency's safety office warning that reversing the airflows in the lab area "represents an extreme departure from the existing design and operation" and that the change will result in "no safeguards against flow disturbances." It noted that there was not universal acceptance of "such a radical change" by those involved in the building, including animal staff and researchers working with tuberculosis.

After the air was reversed, air pressure problems developed in some areas resulting in fire code violations. Under certain circumstances, the pressure needed to open doors that scientists and other workers would need to escape through in an emergency is more than three times what the fire code allows, according to a contractor's report from December 2010 and an e-mail from Moss in January 2011.

The report noted: "Also, on some doors the excessive negative pressure prevented the release of the electronic security latch as commanded by the card reader; it was necessary to push/pull the door

inward/outward before turning the handle and opening the door." CDC assumed responsibility for reopening the lab area with the "known code violation" and was going to begin work to address it, the contractor's report said. The CDC wouldn't say whether the problem has been fixed.

CDC considers outside checks on bioterror labs

By Alison Young

USA TODAY

6/25/2012

The Centers for Disease Control and Prevention is considering having U.S. Army scientists or another outside agency inspect its bioterror labs in the wake of a USA TODAY report this month.

The agency plans to install safety equipment to address fire code violations from December 2010 that could trap workers in an emergency, an agency spokesman said Monday.

USA TODAY reported that the agency's \$214 million Emerging Infectious Diseases Laboratory in Atlanta has had repeated problems with airflow systems designed to prevent the release of infectious agents. The lab, also called Building 18, has a secure, high-containment block where experiments can be done on anthrax, monkeypox, dangerous strains of flu and other agents that have the potential to be used as bioterror weapons.

Monday, the U.S. House Energy and Commerce Committee launched a bipartisan investigation and sent the CDC a letter calling for documents and e-mails relating to safety issues in the lab building to be submitted by July 6. The committee is investigating whether the CDC is complying with federal lab safety requirements.

CDC spokesman Tom Skinner said the agency is considering having an outside agency examine safety and security at its lab buildings "to see if there's anything we can and should be doing to make our program even better than it already is." Possible outside agencies include the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) or the lab safety arm of Health Canada, Skinner said. Currently, the CDC inspects itself.

MORE: Read the committee's letter to the CDC

"I can understand how some feel that CDC overseeing itself is a conflict of interest," Skinner said. But he said the agency has a 66-year record of operating labs safely, including Building 18. He said tens of thousands of hours of scientific work have been done in Building 18 without any incidents of infectious agents being released or anybody being sickened. "We have an extraordinary track record for that building as far as safety goes," he said.

Richard Besser, former head of the CDC's Coordinating Office for Terrorism Preparedness and Emergency Response, raised concerns June 13 about the CDC's self-policing in an ABC News report about Building 18's airflow problems. "Laboratory safety is not an area where you want to have this much self-policing. ... There is clearly an appearance of conflict of interest in having the inspection program at CDC given the number of laboratories housed within the agency," said Besser, who is the network's chief health and medical editor. Besser was unavailable for an interview.

Building 18, which opened in 2005, has had a series of safety incidents involving airflow systems since at least 2007. In February, air from inside a potentially contaminated lab briefly blew outward into a "clean" corridor where visitors weren't wearing any protective gear, which raised concern about exposure risks, according to e-mails obtained by USA TODAY. Research animals in the lab had not been infected at the time of the incident, the records say.

CDC engineers have raised written concerns about the air-containment systems since at least 2010. One concern was that negative air pressure could make it difficult for workers to escape in an emergency, requiring three times more force to open a door than the fire code allows.

Skinner said Monday that until recently, officials in the agency's safety office believed the doors weren't in violation because of their interpretation of the fire code.

The CDC is looking for ways to address the problem, including potentially installing emergency crash bars to help open the doors and further educating employees about the problem. Skinner said the issue involves about three of more than 20 doors in the high-containment lab area.

Monday's letter from the House Energy and Commerce Committee was signed by Rep. Fred Upton, R-Mich., the committee chairman; and Reps. Cliff Stearns, R-Fla., chairman of the Subcommittee on Oversight and Investigations; and Michael Burgess, R-Texas, vice chairman of the health subcommittee.

It also is signed by Reps. Henry Waxman of California, the ranking Democrat on the committee; and Diana DeGette of Colorado, the ranking Democrat on the oversight subcommittee.

"The recent reports of potential safety lapses at one of the CDC's most sensitive biolabs are of tremendous concern," Stearns said. "It is troubling that the integrity of this \$214 million facility could be in question, and we must do all that we can to ensure our scientists are safe. Even one incident is too many at Building 18."

Security lapses found at CDC bioterror lab in Atlanta
By Alison Young, USA TODAY
6/27/2012

A federal bioterror laboratory already under investigation by Congress for safety issues has had repeated incidents of security doors left unlocked to an area where experiments occur with dangerous germs, according to internal agency e-mails obtained by USA TODAY. In one incident, an unauthorized employee was discovered inside a restricted area.

A Centers for Disease Control and Prevention spokesman says the unsecured door incidents in 2010 and 2009 inside its Emerging Infectious Diseases Laboratory in Atlanta were "not an acceptable practice of the agency." At no time, though, were bioterror organisms such as anthrax at risk of falling into the wrong hands, he said.

"The doors in question here are but one layer of multiple layers of security when it comes to both the animals and the agents that are worked on," CDC spokesman Tom Skinner said. "The security measures we have in place, without going into detail, make it close to impossible for anyone who doesn't have approved access to the agents to get their hands on them."

MORE: CDC considers outside checks on bioterror labs

The e-mails document doors being left unlocked in the building's high-containment lab block, which includes an animal-holding area and Biosafety Level 3 labs where experiments are done on microbes that can cause serious or potentially fatal diseases and can be spread through the air. Anthrax, monkeypox, dangerous strains of influenza and the SARS virus are examples.

One e-mail by a CDC safety manager describes an unauthorized man discovered in the animal-holding area and multiple doors that were unsecured at the time. Skinner says the man was a CDC scientist but was not immediately able to provide further details about why he was in the restricted area. Skinner said the man was in an outer corridor of the BSL-3 suite of labs.

For safety and security, access to BSL-3 labs is restricted and they are supposed to have special airflow systems designed to help keep organisms inside. Problems with the airflow systems revealed by USA TODAY, including a February incident where air briefly blew out of a lab into a "clean" hallway, prompted the House Energy and Commerce Committee this week to launch a bipartisan investigation into safety issues. The committee is examining whether CDC — which inspects its own labs along with others nationwide that handle bioterror agents — is complying with federal safety requirements at the lab building, also known as CDC Building 18.

E-mails written by CDC Safety and Occupational Health manager Patrick Stockton indicate the lab has had security lapses that Rutgers University biosafety expert Richard Ebright said may be a "major violation" of security standards for labs that work with potential bioterror agents.

In a November 2009 e-mail, Stockton wrote to several CDC officials involved with Building 18's high-containment laboratory area: "We are continuing to have some difficulties with doors remaining unsecured in the (high-containment lab) area. ... If we continue to have issues, we will need to begin looking at individual access rights for these doors." The particular issue involved expansion sections of the doors, used to accommodate large pieces of equipment. The "through-bolts are not being re-engaged, and the doors are remaining unsecured," Stockton wrote.

Five months later, the expansion doors continued to be left unlatched and unsecured. According to an April 29, 2010, e-mail to more than a dozen CDC officials involved with the lab building, Stockton wrote that earlier that day "an individual with no access and no escort" was found in the research animal-holding area of the high-containment lab area.

The e-mail continued: "He did not have access and at this point we are not sure how he got there." Stockton wrote that he talked to program and animal staff and "no one from their programs let this person in." CDC's Office of Security and Emergency Preparedness, which is a liaison to the Department of Homeland Security, was investigating, the e-mail said. Homeland Security officials did not respond to questions about the CDC security incidents.

Stockton's e-mail says that after the incident he and the building's high-containment lab manager,

Anthony Sanchez, walked the entire high-containment block and found two doors unsecured. "This can certainly happen by mistake on occasion but we have addressed this issue in the past and now it seems to be a common failure point. ... It is imperative that all doors leading to high containment remain secured," Stockton wrote.

Stockton and Sanchez didn't grant interviews. CDC spokesman Skinner said: "Doors being left open by staff is not a standard practice. It's unacceptable, and our safety office has sent out numerous reminders to staff of the importance of staff practicing good physical security."

Skinner said he is unaware of any other door security incidents after the one in April 2010. He emphasized that multiple layers of security in the building would have prevented any unauthorized person from accessing germs that hold the potential to be used as bioterror weapons. "The bottom line is, worker safety and the public safety were never compromised," he said.

Ebright, of Rutgers University, expressed concern about the repeated issues revealed in news reports about Building 18 since the \$214 million building opened in 2005, including articles in 2007 about backup generators that failed to keep airflow systems working during a power outage, and in 2008 about a high-containment lab door that the CDC sealed with duct tape after an incident where an airflow system malfunctioned and sent potentially contaminated air into a "clean" corridor.

The "documents you have obtained over the past several years make it clear that there has been a pattern of corner-cutting and negligence at CDC biocontainment facilities —starting with the failure to include provisions for emergency backup power, and encompassing inadequate door seals, improper airflow, jury-rigged repairs, and unsecured access points," Ebright said.

If the security issues described in Stockton's 2010 e-mail continue and bioterror agents are being used in that area, Ebright said, "then heads should fall."

The CDC currently is responsible for inspecting the safety and security of its labs that work with bioterror agents. Skinner said CDC has a 66-year record of operating its labs safely.

The CDC said this week, in the wake of USA TODAY's reports, that it is considering having its labs' safety reviewed by an outside agency, such as the U.S. Army Medical Research Institute for Infectious Diseases (USAMRIID).

Biosafety and biosecurity concerns have been the subject of previous congressional concerns. A 2009 report by the U.S. Government Accountability Office, the investigative arm of Congress, examined the potential risks posed by the growing number of high-containment labs doing research on potential bioterror agents. It found that while lab accidents are rare, they do occur, primarily because of human error and systems failures.

It also noted that insiders working in the labs can pose risks, pointing to the Federal Bureau of Investigation's allegation that Bruce Ivins, a scientist at USAMRIID in Fort Detrick, Md., was the "sole culprit" in the 2001 anthrax attacks. While he was under investigation in 2008, Ivins died of a drug overdose.

"There are arguably two aspects to insider risk: the motive of the insider and the ability to misuse material and laboratory facilities," the GAO wrote in its report.

CDC bioterror labs cited for security flaws in audits
Alison Young, USA TODAY
February 26, 2013

Laboratories at the Centers for Disease Control and Prevention have been repeatedly cited in private government audits for failing to properly secure potential bioterror agents such as anthrax and plague, and not training employees who work with them, according to "restricted" government watchdog reports obtained by USA TODAY.

"These weaknesses could have compromised [CDC's] ability to safeguard select agents from accidental or intentional loss and to ensure the safety of individuals," according to a 2010 report by the Department of Health and Human Services' inspector general.

The IG probed federal lab security after a scientist at an Army lab was implicated in the anthrax attacks in 2001. The IG also noted problems with CDC lab security in reports from 2009 and 2008.

The reports — which are prompting concern among some key members of Congress — offer a rare window into the CDC's performance on safety and security issues when working with the world's most dangerous pathogens.

The CDC is the main federal agency that oversees government and private bioterror lab safety involving agents dangerous to people, but it refuses to release copies of its lab inspection reports. The IG's office released its reports to USA TODAY in response to a Freedom of Information Act request.

CDC officials said nobody was endangered because their labs have redundant layers of safety and security to protect employees and the public. When issues arise, they are fixed immediately, said Joseph Henderson, director of the CDC's Office of Safety, Security and Asset Management. "We always take it seriously," he said. "We strive for perfection."

The issues cited in the IG reports are "troubling," said U.S. Rep. Fred Upton, chairman of the House Committee on Energy and Commerce. His committee has been examining federal regulation of bioterror labs in the wake of USA TODAY reports last summer about incidents at CDC labs in Atlanta of security doors left unlocked and issues with airflow systems that help prevent the release of infectious agents. The newspaper's earlier reports, which involved incidents in 2009-2012, were based on leaked internal e-mails and other records.

The IG reports were heavily redacted by government officials because they contain "restricted, sensitive information." Still Upton, R-Mich., said they "show the need for better scrutiny over the handling of select agents ... and we intend to immediately look into the issues raised."

The reports also concerned U.S. Rep. Henry Waxman of California, the ranking Democrat on the committee. He said, "There appears to be long-standing and recurring problems at CDC's labs which underscore the need to increase oversight and to ensure that appropriate action is taken to correct these problems permanently."

The issues cited in the IG's audits include:

Failing to ensure the physical security of bioterror agents or restrict access to approved individuals. The 2009 report cites coding on electronic cards that allowed overly broad access to approved workers, allowing them wide access to all bioterror research areas, rather than just the specific areas or specimen freezers for their projects. Most of the details in the 2010 report were redacted.

Failing to ensure that those working with and around potential bioterror agents have received required training. The 2010 report says auditors couldn't verify that 10 of 30 employees sampled had the required training. The 2009 report says the labs "did not provide biosafety and security training to 88 of 168 approved individuals" before they were given access to work areas for bioterror agents.

Not ensuring that only approved individuals accepted packages containing potential bioterror agents arriving from other outside labs. The 2010 audit identified six unapproved people — five from a delivery contractor and one security guard — who received and signed for the packages. The 2008 report, which focused on security of arriving packages, also identified issues.

In 2008, the FBI implicated a microbiologist working at an Army biodefense lab as being responsible for the anthrax letter attacks, which killed five and sickened 17. The scientist, Bruce Ivins, took a fatal

overdose of Tylenol while under scrutiny.

It is not clear which germs or toxins, known as "select agents" in federal regulations, were involved in the CDC incidents that occurred from 2005 to 2009. Select agents are all dangerous pathogens and include the ebola virus, monkeypox virus, the toxin that causes botulism and ricin, a deadly poison that made headlines in 2003 after a potential London terror attack was foiled.

Although the locations of the CDC labs examined by the IG's auditors were redacted from the reports, Henderson said the 2010 and 2008 audits involved labs on the CDC's main campus in Atlanta, and the 2009 audit was of the agency's labs in Fort Collins, Colo.

Rutgers university biosafety expert Richard Ebright, who reviewed the IG reports at USA TODAY's request, said the issues cited are significant and repeated. "There is no evidence of improvement. Some of the same kinds of violations occurred repeatedly over the three-year review period," he said. "It is ironic that the institution that sets U.S. standards for safety and security of work with human pathogens fails to meet its own standards."

In the wake of USA TODAY's reports last June and concerns about the CDC policing itself, the CDC agreed last August to have its labs inspected by bioterror lab experts from the U.S. Department of Agriculture. The USDA has inspected CDC labs twice, said CDC spokesman Tom Skinner, and inspections will occur every 12 to 18 months.

The CDC would not share copies of its most recent inspection reports, saying it is agency policy not to release them for security reasons. Yet to document that CDC had corrected airflow issues at its Emerging Infectious Diseases Laboratory in Atlanta, the agency on Friday provided USA TODAY a copy of an external lab safety review done at the CDC's request by biosafety experts from Canada's public health agency. The Canadian review at the \$214 million 11-story lab complex known as Building 18, says it found no issues of "non-compliance" that pose health and safety risks.

The CDC has not responded to USA TODAY's FOIA requests filed eight months ago for copies of its inspection reports for Building 18's labs, nor has it responded to requests for documents about the building's lab security and airflow incidents.