

September 2009

HIGH-CONTAINMENT LABORATORIES

National Strategy for Oversight Is Needed



GAO

Accountability * Integrity * Reliability



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 burnetti* (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

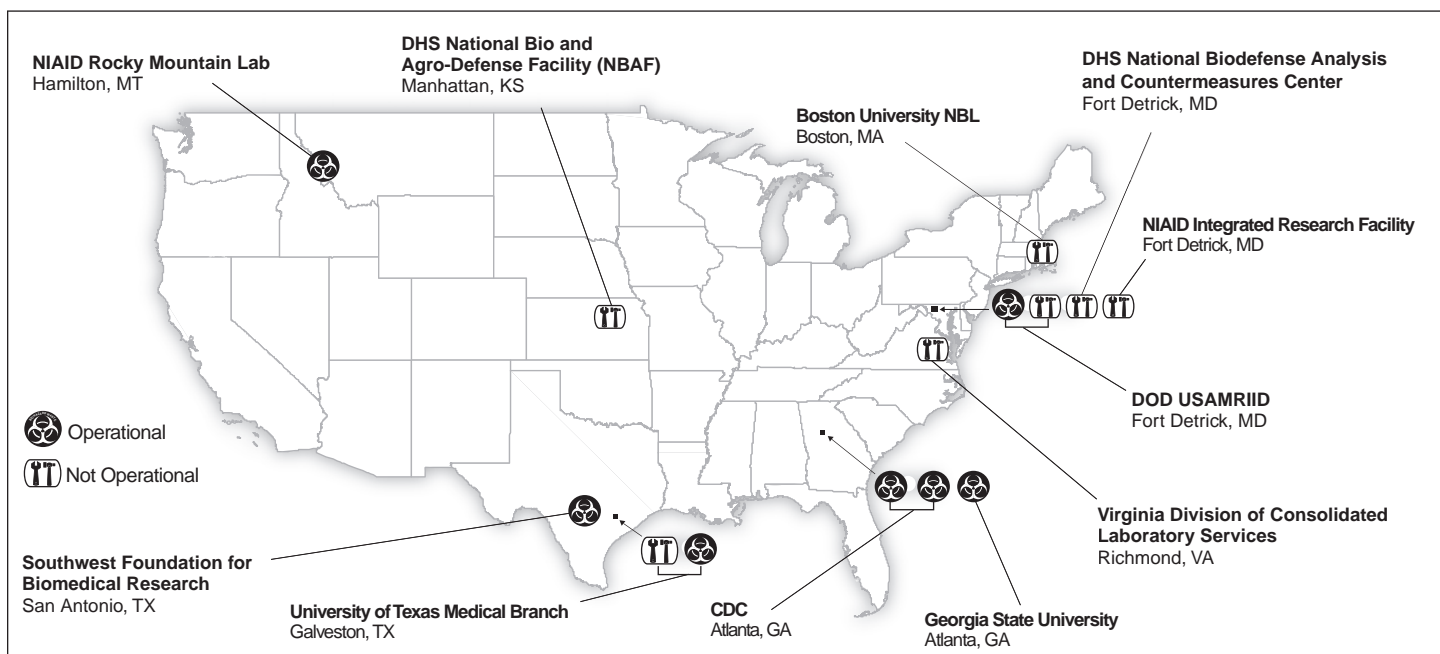
The total number of BSL-4 laboratories will increase from 7 to 13 when these laboratories become operational.²⁶ The locations of the BSL-4

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.

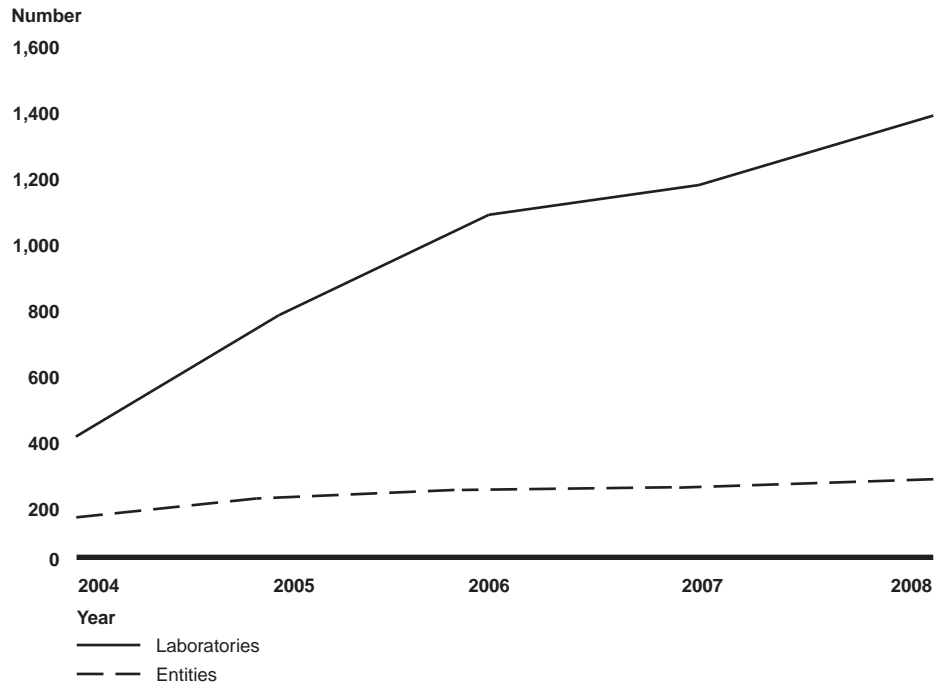
In April 2007, we conducted a Web-based survey—based on a search of publicly available sources—of contacts knowledgeable about high-containment laboratories (for example, biosafety officers).²⁷ A number of respondents who stated that their institutions had high-containment laboratories said that their 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:

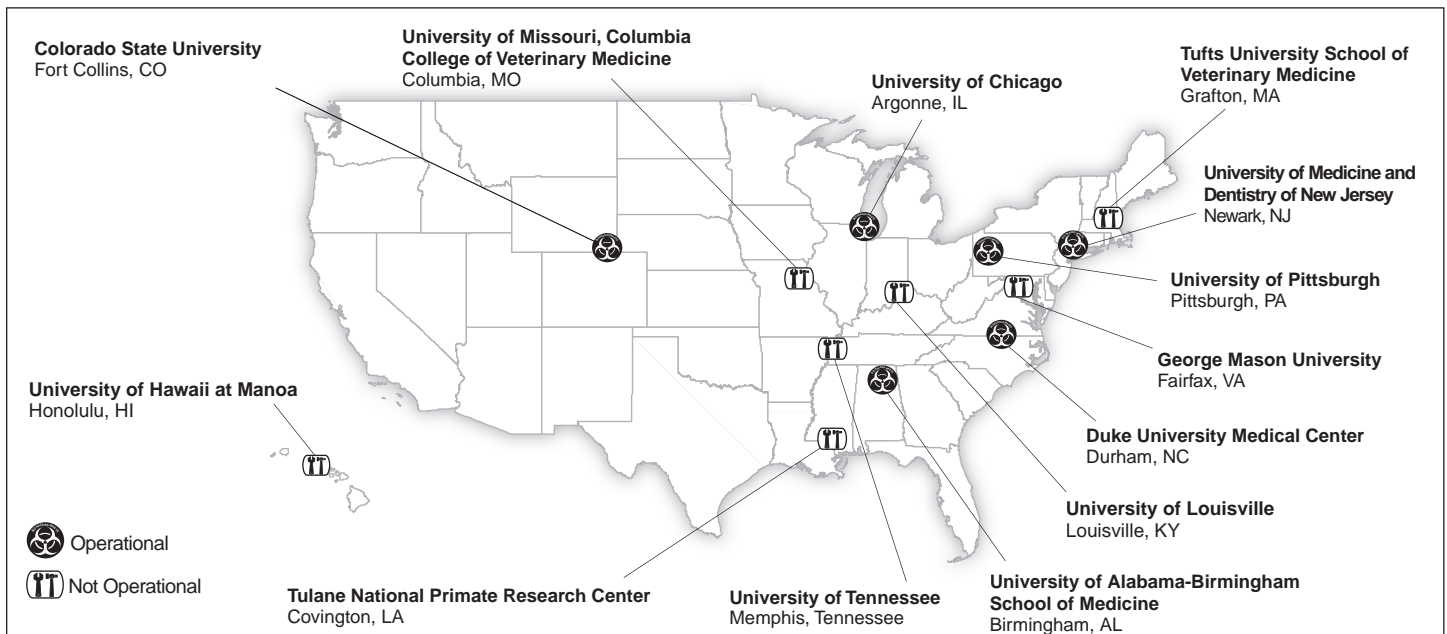
- (1) Colorado State University, Fort Collins, Colorado;
- (2) Duke University Medical Center, Durham, North Carolina;
- (3) George Mason University, Fairfax, Virginia;
- (4) University of Hawaii, Manoa, Hawaii;
- (5) University of Louisville, Louisville, Kentucky;
- (6) University of Medicine and Dentistry 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
Sclerophthora 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-CONTAINMENT 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-CONTAMINMENT 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

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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.

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