



Testimony
Before the Subcommittee on Oversight
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Representatives

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HIGH- CONTAINMENT LABORATORIES

Actions Needed to Mitigate Risk of Potential Exposure and Release of Dangerous Pathogens

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Chairman Murphy, Ranking Member DeGette, and Members of the Subcommittee:

We are pleased to be here today to discuss our work on high-containment laboratories, with a particular focus on the inactivation of pathogens, which is the removal of a pathogen's hazardous effects while retaining characteristics of interest for future use.¹ A number of concerns have been raised in recent years about the biological safety and security of pathogens in high-containment laboratories, and we have previously reported on these issues. For example, in 2009, we found that oversight of high-containment laboratories is duplicative and fragmented and relies on self-policing.² Agencies have made some progress in implementing many of our past recommendations, but the United States still does not have a single entity charged with overseeing the implementation of a national strategy to identify the aggregate risks associated with the expansion of the number of high-containment laboratories and the nature and extent of oversight needed.

Our testimony today summarizes our August 2016 report entitled *High-Containment Laboratories: Improved Oversight of Dangerous Pathogens Needed to Mitigate Risk*.³ In May 2015, the Department of Defense discovered that one of its laboratories had inadvertently sent live *Bacillus anthracis*, the bacterium that causes anthrax, to almost 200 laboratories worldwide over the course of 12 years. Several other incidents involving incomplete inactivation of pathogens have occurred in the United States in recent years, potentially exposing people to dangerous pathogens that can cause infectious diseases.⁴

¹Inactivation is a process used in laboratories to render pathogens unable to cause disease but still retaining characteristics of interest for future use, such as for vaccine development.

²GAO, *High-Containment Laboratories: National Strategy for Oversight Is Needed*, [GAO-09-574](#) (Washington, D.C.: Sept. 21, 2009).

³GAO, *High-Containment Laboratories: Improved Oversight of Dangerous Pathogens Needed to Mitigate Risk*, GAO-16-642 (Washington, D.C.: Aug. 30, 2016).

⁴Incidents involving incomplete inactivation include incidents in which researchers had intended to inactivate samples before removing them from containment but failed to do so because of an issue with the inactivation method, a mix-up of samples, or another unforeseen event.

Researchers in high-containment laboratories may perform inactivation for a variety of reasons, such as to develop vaccines or perform diagnostic testing, and may perform inactivation on a variety of pathogens, including pathogens classified as select agents. Select agents are pathogens, such as bacteria, viruses, and toxins, that have the potential to pose a severe threat to human, animal, or plant health and safety, or to animal or plant products.⁵ The Federal Select Agent Program (Select Agent Program) regulates the possession, use, and transfer of select agents and is comprised of the Department of Health and Human Services' (HHS) Centers for Disease Control and Prevention's (CDC) Division of Select Agents and Toxins and the Department of Agriculture's (USDA) Animal and Plant Health Inspection Service's (APHIS) Agriculture Select Agent Services. These agencies are responsible for providing oversight and ensuring that high-containment laboratories that work with select agents comply with relevant regulations.⁶ In addition, the National Institutes of Health (NIH) provides oversight and guidance for working with pathogens that contain recombinant or synthetic nucleic acid molecules.⁷

This testimony addresses (1) the extent to which incidents involving incomplete inactivation occurred from 2003 through 2015, (2) any challenges that may affect the implementation of inactivation in high-containment laboratories, and (3) the extent to which the Select Agent Program referred violations and enforced regulations related to incidents involving incomplete inactivation.

⁵As of August 2016, 65 select agents or toxins have been determined to have the potential to pose a severe threat to human, animal, or plant health, or to animal or plant products. In this testimony, the term "select agents" encompasses both select agents and toxins.

⁶42 C.F.R. Part 73 (CDC); 7 C.F.R. Part 331 (APHIS-plant); 9 C.F.R. Part 121 (APHIS-animal).

⁷Department of Health and Human Services, National Institutes of Health, *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* (Bethesda, Md.: April 2016). NIH defines recombinant or synthetic nucleic acid molecules as either (1) molecules that are constructed by joining nucleic acid molecules and can replicate in a living cell or (2) nucleic acid molecules that are synthesized chemically or by other means. Researchers routinely generate pathogens containing recombinant or synthetic nucleic acid molecules for a variety of purposes, including the creation of vaccines using recombinant material. For the purpose of this testimony, the term "recombinant pathogens" refers to pathogens that contain molecules that are constructed by joining different nucleic acid molecules together (recombinant) or completely new nucleic acid molecules (synthetic).

For our August 2016 report, we examined the implementation of inactivation at federal, academic, and private high-containment laboratories in the United States, including incidents involving incomplete inactivation. We convened, with the assistance of the National Academy of Sciences, a meeting with experts to discuss issues related to the inactivation of pathogens in high-containment laboratories. To evaluate the extent to which incidents involving incomplete inactivation occurred, we analyzed documentation on incidents reported to the Select Agent Program and NIH from 2003 through 2015 and interviewed agency officials. During interviews with agency officials and our expert meeting, we asked about challenges and safeguards associated with the implementation of inactivation in high-containment laboratories. We also reviewed Select Agent Program guidance and inspection documents and interviewed agency officials regarding the steps the program had taken to refer violations and enforce regulations related to incidents involving incomplete inactivation. Additional information on our scope and methodology is available in our report. The work upon which this testimony is based was performed in accordance with generally accepted government auditing standards.

The Total Number of Incidents Involving Incomplete Inactivation of Pathogens Is Unknown

The total number of incidents involving incomplete inactivation that occurred from 2003 through 2015 is unknown for three reasons: (1) the inability to easily identify incidents involving incomplete inactivation in incident databases; (2) the absence of reporting requirements for pathogens that are not select agents; and (3) the absence of a clear, consistent definition of inactivation.

First, we found that the Select Agent Program and NIH do not have the ability to easily identify incidents involving incomplete inactivation because their incident reporting forms are not structured to specifically identify this type of incident. As a result, neither the Select Agent Program nor NIH (for the oversight of recombinant pathogens) was able to provide us with an accurate number of all incidents involving incomplete inactivation that occurred from 2003 through 2015. We identified additional incidents that the Select Agent Program and NIH did not initially identify.

Second, we found that federal incident reporting, in general, is required only for (1) incidents that involve select agents, which are reportable to the Select Agent Program, and (2) incidents that involve recombinant pathogens, which are reportable to NIH. Thus, incidents involving incomplete inactivation of pathogens that are neither select agents nor recombinant pathogens, such as West Nile virus or the bacteria that

causes tuberculosis, are generally not required to be reported to any federal agency.⁸

Third, we found that there is currently no clear and consistent definition of inactivation in guidance or regulations issued by the Select Agent Program and NIH.⁹ As a result, researchers may not consistently define inactivation, which potentially affects how and when they report incidents involving incomplete inactivation. Moreover, experts at our meeting noted that this can make it difficult to understand when an incident occurs. These experts stated that there is a need for a clear, consistent definition of inactivation across key federal guidance documents, and our past work has also shown that the use of standardized definitions is key to ensuring that information is reported consistently.¹⁰

Without the ability to easily identify incidents involving incomplete inactivation on reporting forms, the Select Agent Program and NIH are unable to easily search their respective databases to determine the frequency and causes of incidents related to the pathogens they regulate. In addition, without a clear and consistent definition of inactivation across key federal guidance, researchers may not know when to include incomplete inactivation in an incident report, potentially affecting the number of incidents reported. We concluded that, collectively, these issues prevent the Select Agent Program and NIH from knowing the extent to which incomplete inactivation occurs and whether incidents are properly identified, analyzed, and addressed. Not knowing the magnitude of the problem may inhibit agencies' ability to achieve program missions

⁸As a way to address the issue of incident reporting in a broader scope, we previously recommended in a March 2016 report that federal high-containment laboratories report all incidents, whether they involve select agents or not, to senior agency officials. GAO, *High-Containment Laboratories: Comprehensive and Up-to-Date Policies and Stronger Oversight Mechanisms Needed to Improve Safety*, [GAO-16-305](#) (Washington, D.C.: Mar. 21, 2016).

⁹These guidance documents do include some information on inactivation but do not include a definition of it.

¹⁰Our prior work has found that metrics should be reported in a consistent fashion, and that a key part of consistent reporting is ensuring that standardized definitions, methodologies, and procedures will be used. In addition, our prior work has found that inconsistent definitions limit the comparability of programs across agencies. See GAO, *Defense Inventory: Actions Underway to Implement Improvement Plan, but Steps Needed to Enhance Efforts*, [GAO-12-493](#) (Washington, D.C.: May 3, 2012).

of investigating any incidents in which noncompliance may have occurred.

In our report, we recommended that the agencies develop clear definitions of inactivation for use within their respective guidance documents. We also recommended that they revise reporting forms to help identify when incidents involving incomplete inactivation occur and analyze the information reported to help identify the causes of incomplete inactivation to mitigate the risk of future incidents. HHS and USDA agreed with our recommendations and noted steps they were taking to address them. For example, CDC and APHIS are proposing revisions to the select agent regulations to include a definition of inactivation and are planning to update their reporting forms.

Gaps in Science and Limited Guidance Affect the Implementation of Inactivation in High-Containment Laboratories

Several challenges affect the implementation of inactivation in high-containment laboratories, including (1) limited scientific information for developing and implementing inactivation protocols,¹¹ (2) limited federal guidance for developing inactivation protocols, (3) inconsistent implementation of safeguards to help ensure inactivation is properly conducted, and (4) varied documentation requirements for shipping inactivated material. Experts in our meeting stated that such challenges may affect laboratories' ability to mitigate the risk of incomplete inactivation.

First, we found that insufficient scientific information exists for developing and implementing inactivation protocols. This could result in incomplete inactivation, according to peer-reviewed literature and our group of experts. Examples of insufficient scientific information include a lack of understanding about (1) mechanisms of inactivation, (2) the ability of some pathogens to repair themselves after inactivation, and (3) viability testing (a procedure to determine the extent to which viable pathogens remain in a sample after an inactivation process).

Second, we found that federal guidance for developing and validating inactivation protocols is limited. Major sources for technical guidance that researchers commonly use—such as NIH guidelines and Select Agent Program guidance—provide little detailed information on development

¹¹A protocol is a detailed plan for a scientific procedure.

and validation of inactivation protocols. In lieu of guidance, we found that researchers in laboratories we visited often developed inactivation protocols at a laboratory level and that protocols sometimes varied within the same department, agency, or laboratory, which may increase the risk of incomplete inactivation. We concluded that without more comprehensive and consistent federal guidance on the development and validation of inactivation protocols, protocols will vary in their scientific soundness and effectiveness, increasing the risk that inactivation may not be achieved.

Third, we found that the high-containment laboratories that we visited did not consistently apply safeguards when conducting inactivation, and there is limited federal guidance on doing so. Examples of safeguards that were inconsistently applied at these laboratories included conducting viability testing following inactivation procedures, implementing verification mechanisms to ensure inactivation protocols are followed, and sharing lessons learned.

Fourth, according to experts from our meeting, documenting the shipment of inactivated pathogens provides an important safeguard if the pathogen is determined to be still viable and needs to be destroyed to prevent potential exposures or release. However, we found through our review of agency documents and interviews with agency officials that laboratories vary in their documentation requirements for shipping inactivated pathogens. Without guidance for documenting the shipment of inactivated pathogens, laboratories are at risk of being unable to locate shipped pathogens in a timely manner, which is important if material thought to be inactivated is determined to still be viable.

In our report, we recommended that the agencies take several steps to address these findings. First, we recommended that the Secretaries of Health and Human Services and Agriculture coordinate research efforts and take actions to help close gaps in the science of inactivation and viability testing. Second, we recommended that the agencies create comprehensive and consistent guidance for the development, validation, and implementation of inactivation protocols, including the application of safeguards. Third, we recommended that guidance on documenting the shipment of inactivated material be developed. HHS and USDA agreed with these recommendations and described steps they are taking to address them. For example, HHS and USDA stated that they are developing a federally supported program to improve laboratory biological safety that will include examination of gaps related to inactivation. In addition, for the Select Agent Program the agencies said they plan to

develop guidance to assist with the development and implementation of inactivation protocols and viability testing.

The Select Agent Program Inconsistently Referred Violations and Enforced Regulations Related to Incidents Involving Incomplete Inactivation

The two agencies that comprise the Select Agent Program—CDC and APHIS—did not consistently refer incidents involving incomplete inactivation for further investigation and enforcement to the HHS Office of Inspector General or APHIS’s Investigative and Enforcement Services. For example, the CDC component of the program referred a number of incidents involving incomplete inactivation that it investigated at high-containment laboratories between 2004 and 2015 to the Office of Inspector General. In contrast, the APHIS component of the program investigated two 2014 incidents at CDC laboratories involving incomplete inactivation that it did not refer to its Investigative and Enforcement Services.¹² We found that it was unclear why some incidents were referred and enforced and not others.

According to an interagency memorandum of understanding regarding the Select Agent Program, CDC and APHIS should maintain consistency in the application and enforcement of the select agent and toxin regulations. We found, however, that CDC and APHIS did not use the same set of criteria for referring violations for investigation by the HHS Office of Inspector General or APHIS’s Investigative and Enforcement Services. Moreover, they did not clearly document the bases for referring or not referring violations. In addition, it was unclear why the Select Agent Program took certain administrative actions, such as revoking or suspending an entity’s registration to possess select agents or requiring a corrective action plan, in response to some violations and not others. The Select Agent Program recently took some steps to increase consistency in the application and enforcement of the select agent regulations. However, the extent to which these steps will improve the understanding and transparency of the program’s enforcement is not yet clear. Without consistent criteria and documentation of decisions for referring violations and enforcing regulations related to incidents involving incomplete inactivation, the Select Agent Program will not have reasonable assurance that its regulatory approach to overseeing high-containment laboratories is applied consistently.

¹²Beginning in October 2012, CDC and APHIS agreed that APHIS will lead inspections of CDC laboratories and CDC will lead inspections of APHIS laboratories.

In our report, we recommended that CDC and APHIS develop and implement consistent criteria and documentation requirements for referring violations to investigative entities and enforcing regulations related to incidents involving incomplete inactivation. HHS and USDA agreed with this recommendation and described steps they recently took, or are planning to take, to increase consistency in the application and enforcement of the select agent regulations. For example, they said that for the Select Agent Program they have developed a draft document that provides guidance on when to refer violations and options for enforcement actions but they did not provide a time frame for finalizing and implementing the draft document.

In conclusion, these inconsistencies, in conjunction with our past work, also raise larger questions about the potential limitations of the Select Agent Program as a whole to effectively and independently oversee high-containment laboratories, both within HHS and across other federal agencies. Select Agent Program officials and an expert from our group noted that the Select Agent Program is independent in its oversight of HHS labs since it organizationally exists in a separate part of the department from the HHS agencies that have high-containment laboratories. However, as we have noted in our prior work, existing federal oversight of high-containment laboratories is fragmented and largely self-policing, raising questions about whether the government framework and oversight are adequate.

Chairman Murphy, Ranking Member DeGette, and Members of the Subcommittee, this concludes our prepared statement. We would be pleased to respond to any questions that you may have at this time.

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