Written Testimony
House Committee on Energy and Commerce, Subcommittee on Oversight and Investigations

Bioresearch Labs and Inactivation of Dangerous Pathogens

Statement of

Stephan S. Monroe, PhD

Associate Director for Laboratory Science and Safety
Centers for Disease Control and Prevention
Department of Health and Human Services

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Introduction

Good morning Chairman Murphy, Ranking Member DeGette, and Members of the Subcommittee. Thank you for the opportunity to testify before you again about the Centers for Disease Control and Prevention's (CDC) ongoing efforts to strengthen and enhance the quality and safety of the Agency's laboratories. I am Dr. Steve Monroe, the CDC Associate Director for Laboratory Science and Safety. My role and office were created last year to serve as the single point of accountability for laboratory science and safety at CDC, and I report directly to the Director, Dr. Tom Frieden. My office provides internal oversight to CDC's laboratories and is distinct from CDC's regulatory arm in the Division of Select Agents and Toxins which, along with the Animal and Plant Health Inspection Service at the U.S. Department of Agriculture, forms the Federal Select Agent Program and regulates the possession, use, and transfer of biological select agents and toxins.

CDC's laboratories serve an essential role in identifying and responding to threats to the public's health. Working with dangerous pathogens is a necessary and vital part of this task, and the effective inactivation and attenuation of pathogens is an especially important scientific and safety challenge. My office and CDC leadership are committed to providing our laboratories the support and guidance they need to meet this challenge, and our laboratories have made tremendous progress in doing so over the last two years.

Effective inactivation makes laboratories safer. A central tenet of laboratory safety is to assess, manage, and mitigate risk whenever possible. One fundamental way to do this is to work with pathogens that present the lowest level of risk without compromising the ultimate goals of a laboratory's work. This often will require working with inactivated or attenuated pathogens that pose less risk while still preserving the biological characteristics needed for scientific study.

Inactivation also expands the reach of public health laboratories. Inactivation and attenuation allow laboratories to advance public health work on pathogens outside of resource-intensive high-containment laboratories—an invaluable capacity when marshalling a public health response. Inactivated and attenuated viral and bacterial strains also are indispensable to vaccine research, the creation of positive control samples for diagnostic assays, and innumerable other scientific and public health applications. But for all the significant scientific and safety benefits provided by inactivation and attenuation, it is critical that when laboratories inactivate pathogens they do so safely, completely, and verifiably.

As this Subcommittee is aware, in 2014 there were a number of unacceptable safety incidents at CDC. The most prominent of these incidents involved the incomplete inactivation of *Bacillus anthracis* in a CDC laboratory that potentially exposed CDC staff to live bacterial spores. This incident was the seminal event that led to major safety reforms within CDC laboratories, including the creation of my position and the establishment of my office. Given this history, the seriousness with which CDC, and I, take the safe inactivation of pathogens in our laboratories cannot be overstated.

Today, I want to speak to CDC's efforts to date to ensure that when CDC's laboratories inactivate and attenuate pathogens and move them from high containment that we do so safely and effectively. In particular, I will highlight the four primary ways we advance this goal: through oversight, guidance, policy, and innovation.

Oversight

The Government Accountability Office (GAO) report emphasizes regulatory approaches to ensuring appropriate inactivation, and CDC agrees that regulations are invaluable to help ensure appropriate laboratory safety and security when working with pathogens. Oversight and regulatory compliance are fundamental to our approach to laboratory safety at CDC. One of the key reforms in the wake of the 2014 incidents was the consolidation of all internal oversight for the safe operation of CDC's

laboratories —including compliance with the requirements of the select agent and toxins program, biosafety, chemical safety, and radiation safety—in the Office of the Associate Director for Laboratory Science and Safety.

But CDC views safety regulatory requirements as a floor, not a ceiling, for putting the best scientific and safety practices into action, including those for the inactivation and attenuation of pathogens. As an agency, we are striving to go above and beyond what is required by regulation to ensure comprehensive oversight of inactivation practices and protocols. The creation of the CDC's Laboratory Safety Review Board (LSRB) in March 2015 marked an important step forward in CDC's efforts to keep our scientists and laboratories safe.

The Laboratory Safety Review Board was born out of the safety incidents in 2014. Following the anthrax safety incident that year, the CDC Director issued a moratorium on all transfers of biological materials out of Biosafety Level 3 (BSL-3) and BSL-4 laboratories. No CDC laboratory could move materials out of high containment until the specific protocols for those transfers were reviewed and approved by a temporary, newly created internal safety body called the Laboratory Safety Improvement Workgroup, or LSIW.

The LSIW regarded proper inactivation and attenuation as a fundamental part of any transfer protocol. For biological materials to leave BSL-3 or BSL-4 containment, a laboratory had to demonstrate that the pathogen had been killed or attenuated so that the unique protections afforded in a high-containment laboratory were no longer required to work with the pathogen safely. Over the course of four months, the LSIW met almost daily to review and scrutinize the transfer and inactivation protocols of every BSL-3 and BSL-4 laboratory. Those protocols that did not meet the LSIW's standards for completeness and verifiability were rejected and sent back for revision until they met the standards.

The LSIW was a temporary body to guide the Agency's response to the 2014 safety incidents; once the LSIW had completed its work and the transfer moratorium was lifted, CDC set about establishing a permanent body to continue the LSIW's vital function. This body is the Laboratory Safety Review Board, or LSRB. The LSRB is charged with reviewing every protocol for the inactivation and transfer of biological materials out of CDC's BSL-3 and BSL-4 laboratories to lower levels of containment. If a laboratory creates a new protocol or amends an existing one, that protocol must be reviewed and approved by the LSRB. Further, all existing protocols are subject to annual review by the LSRB.

The LSRB examines every part of the transfer and inactivation protocol. Laboratories submitting a protocol to the Board must describe their protocol in detail and provide every standard operating procedure (SOP) relevant to the inactivation and transfer of the pathogens they work with. The LSRB mandates two key steps to check safety- critical control points in the inactivation procedures. First, they must complete a detailed checklist of every procedural step of the inactivation and transfer; and second, they must establish a method of secondary verification of inactivation—that is, a process in which a second person or method verifies that the essential steps of the inactivation were done and done correctly. Secondary verification is a particularly important feature of this process as it provides verifiable evidence (like a second person who observed the inactivation or a label that changes color when a specimen receives an irradiation dose sufficient to inactivate the pathogen) that the inactivation process has been performed according to protocol and has been completed successfully.

The LSRB also requires that CDC laboratories rely on validated, documented methods of inactivation. The Board requires that a laboratory provide peer-reviewed scientific literature documenting the efficacy of its proposed inactivation protocol or that a laboratory perform its own internal testing of the procedure and provide sufficient data to show that it works.

Additionally, CDC recognizes that even the most rigorous and validated protocol is only as good as the people who perform it. That is why the LSRB not only reviews the inactivation protocol but requires an annual competency assessment from every individual who performs inactivation in a CDC BSL-3 or BSL-4 laboratory. Individuals are assessed by a technical monitor (who is also subject to competency assessment) who directly observes the scientist performing the inactivation method, doffing and donning personal protective equipment, decontaminating the work space, and performing any other activities relevant to the inactivation procedure.

Finally, any inactivated biological material that leaves BSL-3 and BSL-4 containment at CDC must be accompanied by a material transfer certificate, which is essentially a death certificate for the pathogen being transferred. These certificates document the method used to inactivate the pathogen and are signed by the preparer of the sample and a secondary verifier attesting to the fact that the protocol was followed. Each certificate is also signed by the laboratory branch chief to ensure laboratory leadership is accountable for the materials leaving their laboratories.

Having seen the LSRB perform its important mandate, I can attest that the Board is exacting in its scrutiny and will send back for revision any protocol that it finds does not meet its standards. The creation of the LSRB is a signature reform of the Agency in the wake of the 2014 incidents and represents a fundamental change in CDC's oversight of the creation and implementation of inactivation protocols.

Guidance

In addition to CDC's direct oversight of inactivation in its laboratories, CDC is also committed to providing scientific guidance both to its own laboratories and to the field generally. CDC is in the process of updating all of its manuals for laboratory safety. In the fall of this year, a new CDC

Biological Safety Manual will be rolled out to all CDC campuses. This manual includes important guidance to accompany agency-level policies regarding the proper use of personal protective equipment, as well as the use of biological risk assessments for experimental laboratory work. This manual will complement new agency-level policies to enhance laboratory safety at all CDC campuses.

CDC also provides safety guidance to external laboratories. The primary instrument for this guidance is a manual created in partnership with the National Institutes of Health (NIH), *Biosafety in Microbiological and Biomedical Laboratories*, or BMBL. BMBL is a comprehensive guide on biosafety practices and policies for laboratories working with pathogens. In recognition of the influence that BMBL's voluntary guidance has with microbiological and biomedical laboratories, the GAO report on inactivation recommended—and CDC and NIH concurred—that the upcoming revision of BMBL include clear definitions of inactivation and include clear and consistent guidance for the development and implementation of inactivation protocols. CDC and NIH are working to incorporate this definition and guidance in the next revision of BMBL.

Policy

In addition to the direct oversight of laboratory safety and inactivation practices and the guidance CDC and NIH provide to the field through the BMBL, CDC is also working to establish agency-wide laboratory safety and quality policies to impact and strengthen inactivation and other crucial safety and quality practices in CDC laboratories.

Policy at the agency level goes beyond the day-to-day oversight of safety and inactivation practices provided by the LSRB and my office; it places these important practices in a broader context by shaping the Agency's overall approach to laboratory quality and safety. Through effective agency-wide policies, we can ensure that inactivation and transfer protocols are part of a larger structure and culture of laboratory safety at the Agency.

For instance, CDC is in the final stages of establishing an agency-wide policy requiring CDC laboratories to conduct a risk assessment for any new process or procedure. This policy will necessitate laboratory scientists to think through steps they can take to reduce and mitigate risk—whether it is substituting an inactivated or less pathogenic organism in an experiment, using evidence-based decontamination procedures, or determining what personal protective equipment is necessary to prevent possible exposures. By making risk assessment a routine practice at the heart of every laboratory's work, this policy will ensure that safety practices like effective inactivation are a foremost priority for laboratories and are reviewed for every new or changed procedure.

Similarly, CDC is finalizing a policy outlining the required steps for the transfer of biological materials between CDC laboratories on the same campus. This policy outlines the specific safeguards laboratories must take to protect against potential hazards while transferring materials and further integrates requirements like material transfer certificates into everyday routine practice. The goal of these and other policies is to ensure that best practices around inactivation and other key safety practices are not just standalone requirements but fully woven into the culture, practices, and policies of the Agency's diverse laboratories.

Innovation

Finally, CDC recognizes that just as the threats to the public's health are never static, we as an agency must be thinking about tomorrow's response to these threats and how to meet these threats safely. This applies equally to inactivation practices. Tomorrow's prevention research may demand new methods of inactivation that preserve structures within a pathogen that we never needed to look at before. The emergence of a new public health threat may require we find ways to inactivate a pathogen on a scale never before required. Or a new method of inactivation may be needed to create a new vaccine.

To promote these and other innovations, my office launched the Laboratory Safety, Science, and Innovation Intramural Research Fund, which is funded with existing agency resources with the office. This fund provides one-time awards to laboratories across the Agency that propose innovative research or solutions to laboratory safety challenges.

Inactivation is a primary subject of many of the funded innovation projects. We are funding projects to pioneer faster, better, and more efficient inactivation of bacteria; compare different heat virus inactivation methods to improve safety and better preserve DNA structures; establish new inactivation methods for Zika virus; and systematically evaluate inactivation procedures for the highest risk viral pathogens. We are also funding a project that looks beyond inactivation by creating non-infectious pseudoviruses for the Middle East Respiratory Syndrome coronavirus and poliovirus, which would help develop safe assays to detect outbreaks of these and other viruses.

Conclusion

Inactivation is not a standalone procedure, isolated from the other work of the laboratory; it is a process integral to a functional culture of laboratory safety and excellence. When inactivation is done correctly, it amplifies the impact of public health laboratories by allowing lower containment laboratories to contribute to the prevention and control of dangerous pathogens. It facilitates breakthroughs in testing assays or vaccines. And it protects the safety of laboratory staff and the public.

When I first appeared before this subcommittee in April of this year, I stated that laboratory safety at CDC is not a single objective that can be accomplished and checked off, but an ongoing commitment to a culture of safety that demands constant and vigilant dedication. Ensuring our laboratories perform effective, verifiable inactivation of pathogens is an especially important example of CDC's commitment to a culture of safety.

This is why CDC has made such concerted efforts to ensure that our laboratories employ the best available science and practices of inactivation. We advance this work by providing oversight and rigorous scrutiny of every inactivation protocol, guidance to both internal and external laboratories through the BMBL, agency-wide policies that codify inactivation's role in a culture of safety, and support for innovations in the science of inactivation. Safer, more effective inactivation is and will remain a priority for CDC and my office. We have made major strides in strengthening the Agency's approach to inactivation practices, and we look forward to continuing to improve our efforts in this area.

Thank you for the opportunity to testify on this important matter. I would be glad to answer any questions you may have.