Written Testimony of Richard H. Ebright

Board of Governors Professor of Chemistry and Chemical Biology, Rutgers University

Laboratory Director, Waksman Institute of Microbiology

Submitted for the Record to the House Energy and Commerce Committee

Subcommittee on Oversight and Investigations

For the Hearing "Review of CDC Anthrax Incident"

July 16, 2014

Mr. Chairman and members of the Committee:

Thank you for inviting me to discuss the 2014 Centers for Disease Control (CDC) anthrax incident and its implications. I am Board of Governors Professor of Chemistry and Chemical Biology at Rutgers, The State University of New Jersey, and Laboratory Director at the Waksman Institute of Microbiology. I direct a biomedical research laboratory and serve as project leader on four National Institutes of Health biomedical research grants. I conduct research on the mechanism of bacterial RNA synthesis and on the development of new antibacterial therapeutic agents able to treat bacterial infections resistant to current drugs. My research involves both priority public health bacterial pathogens (e.g., the pathogens responsible for Staph infections, Strep infections, and tuberculosis) and priority biodefense bacterial pathogens (e.g., the pathogens responsible for anthrax, plague, and tularemia). I am a member of the Institutional Biosafety Committee of Rutgers University and have been a member of the Working Group on Pathogen Security of the state of New Jersey, the Controlling Dangerous Pathogens Project of the Center for International Security Studies, and the Biosecurity Advisory Board of the Center for Civilian Biodefense. Here, I discuss (1) the 2014 CDC anthrax incident, (2) broader biosafety and biosecurity issues at CDC select-agent biocontainment laboratories, and (3) broader biosafety and biosecurity issues at the more than one thousand other government, academic, and corporate bioweapons-agent (select-agent) biocontainment laboratories that are regulated by the CDC and the USDA. My assessments are based on information in published CDC, Health and Human Services Office of Inspector General (HHS OIG), United States Department of Agriculture Office of Inspector General (HHS OIG), and Government Accounting Office (GAO) documents, on published press reports, and on my knowledge of biosafety and biosecurity standards for work with bacterial pathogens.

2014 CDC anthrax incident

The 2014 CDC anthrax incident involved multiple biosafety and biosecurity violations.

The 2014 CDC anthrax incident involved *multiple* violations of biosafety and biosecurity recommendations in each of *three* CDC laboratories (at least seven distinct violations in total). Had any of three violations in one CDC laboratory not occurred, the incident would not have occurred. Had any of four violations in two other CDC laboratories not occurred, the impact of the incident would have been mitigated.

The CDC Bioterrorism Rapid Response and Advanced Technology laboratory (BRRAT) inappropriately chose to use a virulent strain of anthrax bacteria for a project that did not require a virulent strain, inappropriately used a non-standard procedure to inactivate the anthrax bacteria, inappropriately used a non-standard procedure to verify inactivation, and may inappropriately have handled the resulting material in procedures potentially able to aerosolize anthrax bacteria (i.e., preparing and processing a MALDI-TOF plate) without the engineering controls, operating procedures, and personal protective equipment required for a procedure potentially able to aerosolize anthrax bacteria (i.e., level-II or higher biosafety cabinet, gloves, and gown).

BRRAT then distributed samples of the putatively inert, but actually viable, anthrax bacteria to each of two other CDC laboratories (Bacterial Special Pathogens Branch laboratory, BSPB, and Biotechnology Core Facility Branch laboratory, BCFB). Workers in BSPB and BCFB inappropriately assumed, without verification, that the samples were inert and inappropriately handled the material in procedures potentially able to aerosolize anthrax bacteria (i.e., placing a sample under a stream of compressed gas in BSPB and placing a sample on a vortex mixer in BCFB) without the engineering controls, operating procedures, and personal

protective equipment required for procedures potentially able to aerosolize anthrax bacteria (i.e., level-II or higher biosafety cabinet, gloves, and gowns).

As a result, more than 80 individuals were potentially exposed to anthrax bacteria, more than 40 individuals were deemed potentially at risk of infection with anthrax bacteria, and multiple laboratory rooms required closure and decontamination.

.

The 2014 CDC anthrax incident reprised, nearly exactly, a 2004 incident.

The 2014 CDC anthrax incident reprised, nearly exactly, a 2004 incident in which workers at Southern Research Institute (SRI) in Frederick MD used an inappropriate procedure to inactivate a sample of anthrax bacteria, used an inappropriate procedure to verify inactivation, and sent the putatively inert, but actually viable, anthrax bacteria to Children's Hospital Oakland Research Institute (CHORI), in Oakland CA, where eight persons were exposed before learning the anthrax bacteria were viable.

The CDC, as the agency with regulatory responsibility for US work with select agents relevant to human health, investigated the 2004 SRI-CHORI anthrax incident. An article in the June 11, 2004 Washington Post quotes CDC spokesperson Karen Hunter as stating "All I know is that we're working with all the institutes involved to find out what happened and make sure it doesn't happen again."

The CDC published its report on the 2004 SRI-CHORI anthrax incident in 2005.

The 2005 CDC report included revised biosafety and biosecurity recommendations for laboratories preparing inactivated anthrax bacteria ("preparing laboratories") and laboratories using samples of inactivated anthrax bacteria ("research laboratories").

The 2005 CDC report stated that:

"Inactivated suspensions of B. anthracis should be cultured both at the preparing laboratory

before shipment and at the research laboratory several days before use to ensure sterility. Sensitivity of sterility testing might be enhanced by increasing the inoculum size and incubation time, and by inoculating in multiple media, including both solid and broth media. Such procedures would increase the probability of detecting even a small number of viable *B. anthracis* spores.

The 2005 CDC report further stated that:

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

The 2005 CDC report further stated that:

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

Had the CDC implemented the recommendations in its 2005 report on the 2005 SRI-CHORI anthrax incident, the 2014 CDC anthrax incidents would not have occurred.

But the CDC did not implement the recommendations in its 2005 report.

Contrary to the guidance in the 2005 CDC report:

(1) The CDC preparing laboratory (BRRAT) did not perform the standard sterility testing (reducing the incubation time from the standard 48 hours to a non-standard 24 hours), much less the recommended enhanced sterility testing entailing "increasing the inoculum size and incubation time, and by inoculating in multiple media, including both solid and broth media."

(2) The CDC research laboratories (BSPB and BCFB) did not perform any form of sterility testing, much less the recommended enhanced sterility testing entailing "increasing the inoculum size and incubation time, and by inoculating in multiple media, including both solid and broth media."

(3) The CDC research laboratories (BSPB and BCFB) did not "assume that all inactivated *B. anthracis* suspension materials are infectious until inactivation is adequately confirmed."

(4) The CDC research laboratories (BSPB and BCFB) did not, "use BSL-2 procedures [which minimally include class-II biosafety cabinet, gloves, and gown] while performing activities with a high potential for expelling aerosolized spores."

(5) The CDC research laboratories (BSPB and BCFB) appear not to have provided workers with anthrax vaccination as "an additional layer of protection in the event of an unrecognized breach in practices or equipment failure."

The 2014 CDC anthrax incident shows the CDC did not learn from the 2004 incident.

The fact that the CDC in 2014 made the same errors that had been made by SRI-CHORI in 2004 shows that the CDC did not learn from the 2004 SRI-CHORI anthrax incident. The fact that the CDC had investigated the 2004 SRI-CHORI anthrax incident, had issued biosafety and biosecurity recommendations that would have prevented the repetition of such an incident, but then ignored recommendations, makes the repetition of such an incident even more egregious.

Biosafety and biosecurity at CDC select-agent laboratories

The 2014 CDC anthrax incident is not an isolated incident, but is part of a pattern.

The July 11, 2014 CDC report listed multiple other incidents--none previously disclosed to the public--in which CDC laboratories sent putatively inactivated or attenuated, but actually viable and virulent, select agents to other laboratories:. The incidents included:

(1) Shipping DNA from anthrax bacteria that contained viable anthrax bacteria in 2006 (at least two shipments);

(2) Shipping DNA from botulinum-toxin-producing bacteria that contained viable botulinum-toxin-producing bacteria in 2006;

(3) Shipping putatively attenuated, but actually virulent, brucellosis bacteria in 2001-2009 (multiple shipments, starting in 2001 and continuing until at least 2006 and possibly until 2009).

(4) Shipping low-pathogenicity influenza virus contaminated with highly pathogenic avian influenza virus H5N1 in 2014.

These previously undisclosed CDC select-agent incidents are fundamentally similar to the 2014 CDC anthrax incident. In particular, the previously undisclosed 2006 CDC anthrax incidents may be essentially identical to the 2014 CDC anthrax incident..

All of these incidents raise both safety concerns (potential for accidental exposure) and security concerns (potential for unauthorized and undocumented access to select agents). All of these incidents can be inferred to entail similar errors (inappropriate procedures for sample preparation and/or inappropriate procedures for sample verification).

Press reports document engineering flaws and equipment failures.

Press reports from 2007 through the present have described biosafety and biosecurity engineering flaws and equipment failures at CDC select-agent laboratories, including inadequate provisions for emergency backup power (essential to maintain safety and security containment in the event of a power outage), failure to maintain negative-pressure airflow in biocontainment areas (essential to ensure safety and security containment at all times), non-functioning doors between biocontainment areas and corridors, non-functioning door seals between biocontainment areas and corridors, and jury-rigged repairs to door seals with duct tape.

Press reports also have described perceptions of CDC staff that issues were not promptly corrected after informing CDC management.

Press reports document security violations.

Press reports from 2012 through the present have described security violations in CDC select-agent laboratories, including failure to close secure entry doors to select-agent laboratories, failure to latch secure entry doors to select-agent laboratories, failure to assign distinct key codes to key cards for select-agent laboratories, and, in one case, the discovery of an unescorted unauthorized person in a select-agent laboratory..

Press reports also have described perceptions of CDC staff that issues were not promptly corrected after informing CDC management.

HHS OIG audits document procedural and training lapses.

HHS OIG audits of CDC select-agent laboratories in 2008, 2009, and 2010 (the most recent audits released to date) reported substantive violations. The violations included failures to ensure physical security, restrict access, and document inventories. The violations also included

failure to provide required training to workers (with training being unverifiable for 1 in 3 workers in the most recent available report). Perhaps most egregiously, the violations included unauthorized transfers of select agents to other labs or individuals.

The 2008, 2009, and 2010 HHS OIG audits provide no evidence of improvement. Some of the same kinds of violations occurred repeatedly over the three-year period. The most, and the most serious, kinds of violations appear to have occurred in the most recent year of the three-year period,

Highlights 2008, 2009, and 2010 HHS OIG audits are as follows:

(1) 2008 HHS OIG audit

p8: Did not ensure security during transfers to other labs.

(2) 2009 HHS OIG audit

p6: Did not consistently ensure physical security.

p6: Did not consistently ensure required training.

p11: Did not provide required training before access for more than 1 in 2 select-agent workers.

p12: Entered authorization codes that overrode and defeated electronic access controls.

(3) 2010 HHS OIG audit

p5: Did not consistently ensure physical security, restrict access, provide training, document inventories, and ensure security during transfers to other labs.

p13: Required training unverifiable for 1 in 3 select-agent workers.

p13: Even minimal training unverifiable for 1 select-agent worker.

p14: Unauthorized transfers to other labs.

The evidence indicates that the CDC does not adequately ensure biosafety and biosecurity.

The July 11, 2014 CDC report; 2008, 2009, and 2010 HHS OIG audits; and 2007-2014 press reports indicate that the CDC has not adequately ensured biosafety and biosecurity in CDC select-agent laboratories and are consistent with pervasive and systematic violations of biosafety and biosecurity standards in CDC select-agent laboratories.

Biosafety and biosecurity at CDC- and USDA-regulated select-agent laboratories

The CDC and the USDA have regulatory responsibility for biosafety and biosecurity in US select-agent laboratories.

The CDC has regulatory responsibility for biosafety and biosecurity in all US government and non-government laboratories that possess select agents relevant to human health--including CDC select-agent laboratories.

The USDA has regulatory responsibility for biosafety and biosecurity in all other US government and non-government laboratories that possess select agents relevant to agriculture--including USDA select-agent laboratories.

A 2009 GAO report states that, as of 2008, there were 1,362 registered US select-agent high-level biocontainment laboratories:

(1) 395 federal-government select-agent high-level biocontainment laboratories.

(2) 295 state/local-government select-agent high-level biocontainment laboratories.

(3) 474 academic select-agent high-level biocontainment laboratories.

(4) 125 private non-profit select-agent high-level biocontainment laboratories.

(5) 73 private for-profit select-agent high-level biocontainment laboratories.

A 2013 GAO report states that, as of 2010 (the most recent registration data released to date), there were 1,495 registered US select-agent high-level biocontainment laboratories.

The 2009 and 2013 GAO reports note that the number of US select-agent high-level biocontainment laboratories has increased dramatically since 2001.

The CDC and the USDA do not adequately ensure biosafety and biosecurity in US select-agent laboratories.

2006 and 2012 USDA OIG audits documented flaws in biosafety and biosecurity at non-CDC, non-USDA US select-agent laboratories and also documented flaws in the procedures for, and the reliability of, USDA inspections of non-CDC, non-USDA US select-agent laboratories.

The 2012 USDA audit documented four categories of violations that occurred at US select-agent labs and that had not been detected by USDA select-agent inspections:

(1) Transferring select agents, including anthrax bacteria and plague bacteria, to laboratories not authorized to possess select agents.

(2) Allowing access to select agents by persons lacking current security risk assessments.

(3) Allowing persons lacking documented biosafety/biosecurity training to access select agents.

(4) Allowing persons lacking documented biosafety/biosecurity training to oversee institutional select-agent biosafety/biosecurity.

The violations are significant. The first category of violations is especially significant., in that violations in this category allowed access to select agents by unauthorized institutions and individuals and provided opportunities for theft, loss, or release of select agents.

The failure of USDA select-agent inspections to detect the violations also is significant.

The data presented in the 2012 USDA OIG audit suggest that undetected violations at US select-agent institutions are numerous. The USDA OIG audited only seven US select-agent institutions (a very small fraction of all US select-agent institutions). Nevertheless, for just seven audited institutions, the audit identified multiple previously undetected example of violations in each of the above four categories of violations.

The data presented in the 2012 USDA OIG audit further suggest that undetected violations are widespread. All seven audited institutions were found to have previously undetected violations involving access by persons lacking the required training. Four of the seven audited institutions were found to have previously undetected violations involving oversight of institutional select-agent programs by persons lacking the required training. Four of the seven audited institutions were found to have previously undetected violations involving access by persons lacking current security risk assessments.

The data presented in the 2006 and 2012 USDA OIG audits preclude confidence that the Select Agent Rule is being effectively monitored and enforced.

The 2012 USDA OIG report documented multiple instances in which the USDA OIG recommended corrective measures to the USDA Animal and Plant Health Inspection Service (APHIS), the entity that carries out USDA select-agent inspections, but was rebuffed by APHIS. (The report contains a veritable litany of "APHIS does not concur with the recommendation....APHIS does not concur with the recommendation....APHIS does not concur with the recommendation....APHIS does not concur with the recommendation....") The refusal of APHIS to correct, or even to acknowledge, flaws in its inspection process indicates that APHIS does not prioritize ensuring that the Select Agent Rule is being effectively monitored and enforced.

As described in the preceding sections, available evidence indicates that the CDC has not adequately ensured biosafety and biosecurity standards in CDC select-agent laboratories. There is no basis to believe that biosafety and biosecurity standards are higher, or that select-agent inspections are more stringent, at CDC-regulated, non-CDC select-agent laboratories than in CDC select-agent laboratories. There also is no basis to believe that biosafety and biosecurity standards are higher, or that select-agent inspections are more stringent, at CDC-regulated, non-CDC select-agent laboratories than at the USDA-regulated, non-USDA select-agent laboratories analyzed in the 2006 and 2012 USDA OIG audits.

The fact that the CDC and the USDA not only perform and fund select-agent work, but also regulate biosafety and biosecurity for select-agent work, represents a clear conflict of interest. This conflict of interest may at least partly account for the failure of the CDC and the USDA--evident from the data in the HHS OIG and USDA OIG audits--to ensure adequate biosafety and biosecurity in CDC-regulated and USDA-regulated select-agent programs.

Recommendations

- **Laboratories that send or receive inactivated or attenuated anthrax bacteria should implement the recommendations in the 2005 CDC report.**

- **Laboratories that send or receive inactivated or attenuated select-agent pathogens other than anthrax bacteria should implement recommendations analogous to those in the 2005 CDC report.**

- **The CDC should conduct a systematic review of biosafety and biosecurity engineering controls, operating procedures, personal protective equipment, training, and management in CDC select-agent laboratories; (2) report identified deficiencies; and (3) resolve identified deficiencies.**

- **The CDC should require formal risk-benefit assessments--in which biosafety and biosecurity risks are enumerated, benefits are enumerated, benefits are concluded to outweigh risks, and methods to mitigate risks are identified--before authorizing new projects or new protocols in CDC select-agent laboratories.**

- **Regulatory responsibility for biosafety and biosecurity of US select-agent laboratories should be re-assigned from the CDC and the USDA to an independent entity (an entity that neither conducts nor funds select-agent research).**

- **The number of US select-agent laboratories should be sharply reduced (preferably to fewer than 25-50).**

<u>Appendices</u>

Appendix 1: 2014 CDC Report on 2014 CDC Anthrax Incident

Appendix 2: 2005 CDC Report on 2004 SRI/CHORI Anthrax Incident

Appendix 3: 2008 HHS OIG Audit of CDC Select-Agent Programs

Appendix 4: 2009 HHS OIG Audit of CDC Select-Agent Programs

Appendix 5: 2010 HHS OIG Audit of CDC Select-Agent Programs

Appendix 6: 2006 USDA OIG Audit of USDA Select-Agent Programs

Appendix 7: 2012 USDA OIG Audit of USDA Select-Agent Programs

Appendix 8: 2009 GAO Report on High-Level Biocontainment Laboratories

Appendix 9: 2013 GAO Report on High-Level Biocontainment Laboratories

Appendix 10: 2007-2013 Press Reports on CDC Biosafety and Biosecurity