U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON ENERGY AND COMMERCE

TO: Members, Subcommittee on Oversight and Investigations

FROM: Majority Staff

RE: Supplemental Memorandum: Committee Investigation on the 2014 Discovery of Smallpox Vials at the National Institutes of Health, Bethesda, Maryland Campus

I. Introduction

On April 20, 2016, the Subcommittee on Oversight and Investigations will hold a hearing entitled, "How Secure are U.S. Bioresearch Labs? Preventing the Next Safety Lapse." At the hearing, the Government Accountability Office (GAO) will present its report on agency policies on Federal laboratories working with hazardous biological agents, as well as policies related to the oversight of the labs. In addition to the GAO report, the Committee's majority staff has been investigating issues arising from the Food and Drug Administration's (FDA) discovery of twelve "overlooked" cardboard boxes containing 327 vials of laboratory samples – including six vials of *Variola*, the agent of smallpox – in an National Institutes of Health (NIH) building in July 2014. The discovery of the smallpox vials was one of three incidents that led the White House in August 2014 to urge Federal agencies handling select agents to conduct a "safety stand-down" to search their laboratories for unregistered or improperly stored select agents and establish a Federal review to identify improvements in lab safety.

This supplemental memorandum summarizes the majority Committee staff's preliminary observations from additional information obtained in its investigation into the facts and circumstances pertinent to the discovery of the smallpox vials in July 2014. The purpose of the supplemental memorandum is to identify additional issues that should be further investigated by agencies of the Department of Health and Human Services (HHS), and to highlight systemic, cultural, and behavioral factors that may need to be addressed in addition to the policy changes and oversight efforts being implemented by Federal agencies. Over the last decade, the Subcommittee has held several hearings on Federal lab incidents and biosafety. In addition, both the GAO and the HHS Office of Inspector General (OIG) have issued reports highlighting concerns and deficiencies with oversight and compliance of Federal select agent regulations. The hearings and reports show a pattern of recurring issues, of complacency, and a lax culture of safety. The lesson learned from past reviews is that Federal agencies must address cultural factors in addition to its policy and management efforts to ensure the effectiveness of its lab safety programs.

II. Background of the Discovery of Vials Containing Smallpox

On July 1, 2014, in an effort to clean out and organize material in preparation for the move of FDA's laboratories from the NIH campus in Bethesda, Maryland, to the FDA's White Oak, Maryland, campus, an FDA researcher working in Building 29A discovered twelve "overlooked" cardboard boxes in a common cold storage room.[1] The FDA researcher who found the material immediately reported the discovery to the Associate Director for Research at the FDA Center for Biologics Evaluation and Research. The FDA Associate Director for Research then notified the Responsible Official (RO) for the NIH Select Agent Program. The boxes were transferred to the NIH RO, who secured the materials until

[1] In an interview with Committee staff, the FDA researcher stated that he was in the cold room on a daily basis. He said that he first saw the twelve cardboard boxes in question sitting at the end of a shelf when he came to work at Building 29A in 1992 and never opened the boxes until July 1, 2014. The boxes were not hidden behind anything, but the FDA researcher said that the boxes were at the end of a shelf in a corner and could have been overlooked.

the Centers for Disease Control and Prevention (CDC) and the Federal Bureau of Investigation (FBI) removed the contents.

A. The CDC and FBI Joint Investigation

From July 7 to 9, 2014, the CDC and FBI conducted a joint investigation into the discovery of the smallpox vials, reporting their findings to the NIH on August 8, 2014.[2] Although the cold room had the capability of being locked, FDA personnel reported that the room had never been locked to their knowledge. Further, there were no access logs or inventory records for any material or equipment in the cold room where the vials were found. In addition to the vials of smallpox, labels on the other vials indicated other potential select agents such as Q fever and certain Encephalitis viruses. The CDC and FBI concluded that the location of the materials found did not meet the requirements of the select agent regulations, and that there were "significant vulnerabilities with access control and accountably [sic]."[3]

The twelve boxes contained 327 vials of laboratory samples, including six vials of *Variola*, the agent of smallpox. The twelve boxes were marked on the outside with a series of Roman numerals and letters. Based upon the numbering system, CDC and FBI surmised that there may be at least two boxes not accounted for. All other lettering on the outside of the boxes had been previously marked through, but some of the marked out lettering was legible (e.g., "Measles," "Enders strain"). None of the boxes contained information on the source of the material, but dates on the labels ranged from 1946 to 1964. Some of the labels contained possible names or potential sources. FDA researchers told the CDC and FBI that no one was aware of the owner or source of the material.[4]

The FBI and CDC highlighted that FDA personnel did not take any steps to package and transport the vials in a manner sufficient to prevent their release when they moved the vials from building 29A to the NIH RO. The report states:

> [H]ad any of the six glass vials containing the Variola virus been breached, there would have been nothing to contain the agent and prevent its release to the surrounding environment. During the initial inspection of the vials on July 7, 2014 it was noted that one vial labeled *NOR.SPL.ANT* (presumably Normal Spleen Antigen) had been breached. It was not known when this breach occurred, but this could have occurred during the move on July 1, 2014.[5]

The report further noted that the individual who carried the boxes to the NIH RO indicated that she heard the vials clink together as she transported them from building 29A. Subsequent testing of the samples by the CDC showed that the smallpox virus was still viable in two of the six vials.

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[2] Letter from Robbin Weyant, Director, Division of Select Agents and Toxins, Centers for Disease Control and Prevention to Deborah Wilson, Responsible Official, National Institutes of Health (Aug. 8, 2014).
[3] *Id.*
[4] The policy regarding unlabeled cardboard boxes in cold storage rooms at the National Cancer Institute—Frederick was explicit and apparently different from the policy at NIH's Bethesda campus. According to a biosafety technical bulletin on cold rooms and mold issued by NCI-Frederick in November 2011, personnel were advised that "at a minimum," "DO NOT store cardboard, . . . in cold rooms." National Cancer Institute—Frederick, *Biosafety Technical Bulletin: Cold Rooms and Mold* (Nov. 2011) (emphasis in original). Further, the bulletin stated, "Label equipment and any on-going experiments with name, date and responsible Principle[sic] Investigator (PI**). Note: Any unlabeled samples should be discarded by laboratory managers.**" *Id.* (emphasis in original).
[5] Letter from Robbin Weyant, Director, Division of Select Agents and Toxins, Centers for Disease Control and Prevention to Deborah Wilson, Responsible Official, National Institutes of Health 2 (Aug. 8, 2014).

Federal officials familiar with this case believe that no one detected the cardboard boxes since at least 1972 when the FDA became an NIH tenant of Building 29A. In an interview with Committee staff,[6] the FDA researcher who reported the twelve cardboard boxes, and who had worked in the corridor and cold storage room since 1992, stated that he worked in the cold room on a daily basis. He first saw the twelve cardboard boxes in the cold storage room when he began working in Building 29A in 1992. He did not open the boxes until July 1, 2014. The boxes were not hidden behind anything, but the FDA researcher stated that the boxes were at the end of a shelf in a corner, and could have been overlooked. The CDC and FBI identified the following root cause assessment for the incident:

> Failure of past NIH and FDA actions to fully identify and account for material labeled as potentially select agents and toxins on the NIH Bethesda campus, specifically the failure to have oversight and accountability for material in a shared storage space (e.g. walk in cooler) where ownership of the material is not clear or unknown.[7]

On September 8, 2014, the CDC made a referral to the HHS Office of Inspector General (OIG) regarding the smallpox discovery. In the referral, the CDC noted that this referral supplemented other information provided in an April 2012 referral CDC made to the OIG, which was still pending.

As a result, in contravention of the Public Health Security and Bioterrorism Preparedness and Response Act, neither the FDA nor the NIH accounted for the select agents, nor did NIH ever register these select agents as required by the 2002 law.[8] In addition, the United States had committed in a 1979 international agreement that any remaining stock of smallpox vials would be accounted for and stored only at the CDC or at the Vector Institute in Russia. As a result of this discovery, the World Health Organization was notified and invited to come to the U.S. to confirm that the smallpox vials were secured and then destroyed.

In 1995, NIH safety officers received an anonymous tip that a top-ranking official at an NIH lab in a casual conversation years earlier had said there was smallpox in the freezers.[9] The allegation was not substantiated with the particular lab. However, an NIH spokeswoman said, that if smallpox were found, "that would be regarded as a very serious transgression against science," and "it would be taken very seriously."[10]

B. Subsequent Actions

The 2014 smallpox discovery at NIH was one of a series of high-profile mishandlings involving dangerous pathogens at Federal laboratories. The CDC reported three incidents of inadvertent shipments containing highly pathogenic biological agents such as anthrax, Ebola, and H5N1 influenza, in one year alone.[11] In 2015, the Department of Defense (DoD) acknowledged that the Dugway Proving Ground, an

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[6] Interview with [FDA Researcher] conducted by H. Comm. on Energy & Commerce staff, April 6, 2014.
[7] Letter from Robbin Weyant, Director, Division of Select Agents and Toxins, Centers for Disease Control and Prevention to Deborah Wilson, Responsible Official, National Institutes of Health 2 (Aug. 8, 2014).
[8] 42 U.S.C. § 262a.
[9] Justin Gillis, *NIH Denies It Has Smallpox Sample*, WAS. POST, Sept. 25, 1995.
[10] *Id.*
[11] In June 2014, CDC inadvertently transferred live anthrax between CDC labs, resulting in the potential exposure of 81 CDC staff and the closure of a bioterrorism rapid response lab. In the spring of 2014, CDC inadvertently shipped highly pathogenic H5N1 influenza to a USDA lab. CDC staff further did not inform CDC leadership of the incident for two months. In December 2014, CDC inadvertently transferred potentially live Ebola virus from a biosafety level 4 lab to a lower biosafety level 2 lab.

Army facility in Utah, inadvertently shipped live anthrax to a several laboratories. The CDC[12] and DoD conducted internal reviews on each one of these events.[13] In contrast, neither the NIH nor the FDA have conducted an internal review on the discovery of the smallpox vials in 2014.[14]

The smallpox discovery, along with other incidents, led to a sweep of Federal laboratories in the summer and fall of 2014. As a result of the lab sweep at NIH, other select agents, including botulinum, plague, and ricin were found to be improperly stored. On January 15, 2015, CDC made a referral to the OIG about these additional discoveries.

III. Additional Information Discovered during the Committee's Investigation

The Committee launched its investigation into the smallpox discovery at NIH more than two years ago, after examining the series of incidents involving Federal laboratories mishandling dangerous pathogens. On July 28, 2014, the Committee sent requests to the CDC, NIH, and FDA for documents and information relating to the handling of select agents by Federal laboratories and compliance with the Federal Select Agent Program (FSAP).[15] These requests included questions about the smallpox vials and other dangerous pathogens discussed above. To date, the Committee has obtained documents from the NIH, FDA, CDC, and involving safety inspections and external investigations into the smallpox discovery at NIH. Additionally, the Committee has conducted several interviews with FDA and NIH staff directly involved with the 2014 smallpox findings, and has also spoken with senior officials for both FDA and NIH.

In recent months, after learning of a CDC investigation report into the smallpox discovery, the majority Committee staff looked at other elements of the discovery to understand whether the NIH or FDA could have discovered the smallpox vials earlier, and more broadly, what systemic weaknesses in the NIH and FDA lab safety programs indicated by this lapse may remain unaddressed. The Committee has learned that NIH experienced major events in 2011, when it discovered unregistered, antibiotic resistant plague specimens, and in 2012, when it discovered unregistered, antibiotic resistant anthrax, including at an FDA lab in Building 29A. At least one of these specimens was found improperly stored in a hallway freezer in a building on the NIH Bethesda campus. The Committee believes that these discoveries should have spurred NIH and FDA to conduct a comprehensive sweep of all laboratories to ensure that all select agents were properly accounted for and registered. Unfortunately, neither NIH nor

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[12] CDC, *Report on the Potential Exposure to Anthrax* (July 11, 2014); CDC, *Report on the Inadvertent Cross-Contamination and Shipment of a Laboratory Specimen with Influenza Virus H5N1* (August 15, 2014); and CDC, *Report on the Potential Exposure to Ebola Virus* (Feb. 4, 2015).

[13] DOD conducted a particularly robust review of the inadvertent shipment of anthrax from the Dugway Proving Ground that identified the root causes of the incomplete inactivation of anthrax, found other systemic problems in the management of DoD's high-containment laboratories, and proposed steps necessary to fix those problems. The findings were produced in an Army Regulation (AR) 15-6 Investigation Report entitled, *Individual and Institutional Accountability for the Shipment of Viable Bacillus Anthracis From Dugway Proving Groun*d. DoD assigned ten staff members to conduct an internal investigation, during which staff conducted interviews with over eighty individuals, obtained sixty-nine sworn statements, and produced fifty documents classified as evidence to support findings.

[14] NIH and FDA senior officials have informed the Committee via interviews that an internal review has yet to be conducted to avoid interference with the CDC and FBI investigation, and the HHS-OIG pending FSAP investigation. These investigations have been closed. Both agencies have expressed a willingness to conduct internal reviews once notified that external investigations are closed.

[15] The FSAP oversees the possession, use, and transfer of biological select agents and toxins. The program requires that HHS identify a list of organisms and toxins (known as select agents) that potentially could be used for bioterrorist attacks, and currently regulates sixty-five select agents, including smallpox. CDC's Division of Select Agents and Toxins (DSAT) regulates the possession, use, and transfer of biological agents and toxins that could pose a severe threat to public health and safety.

FDA undertook such a sweep until 2014—after the public disclosure of the discovery of the smallpox vials.

A. 2012 Anthrax Discoveries

In 2014, the NIH reported to the Committee that, in February 2012, the NIH found vials of *Bacillus anthracis* spores in an unregistered space in Building 33 on the Bethesda, MD campus during an inspection of a registered laboratory.[16] NIH described the materials discovered:

> The materials were not secured; personnel in the laboratory were not registered to possess this strain of *B. anthracis*; and the material had not been identified to the NIH Select Agent Program. The vials were immediately removed from the freezer and transported to the registered NIH Select Agent Program laboratory. The spores found were from a non-infectious strain, but were still regulated under the Select Agent Regulations.[17]

After this discovery, the NIH initiated a search of all laboratories known to work with any form of anthrax, regulated or unregulated, to ensure that no further anthrax was stored inappropriately. This inspection found regulated anthrax in three other unregistered locations on campus.[18]

The Committee's investigation has recently uncovered additional facts about NIH's prior violations of Federal select agent regulations. The Committee has learned that the discovery of unreported, unregistered anthrax during a laboratory inspection actually resulted from two principal investigators (PIs) self-disclosing their unauthorized work involving antibiotic resistant *Bacillus anthracis* to the NIH Select Agent Program (SAP) on January 26, 2012, during a Select Agent Program retraining.[19] NIH surrendered these vials of *B. anthracis* spores to the FBI Weapons of Mass Destruction Coordinator shortly after they were identified.[20] As a result of this disclosure, NIH SAP conducted a search of twenty-two refrigerators, freezers, and a cold room used by the laboratory of these researchers.[21] It was during this search that NIH discovered the additional vials of anthrax in three unregistered locations. Recent interviews with NIH staff acknowledged that the 2012 laboratory searches only searched registered spaces for anthrax because NIH believed it had no reason to suspect that there was inappropriate storage of other materials.

The Committee further learned that the Select Agent retraining effort in January 2012, in which two NIH PIs self-disclosed select agent material, occurred because of a previous discovery of unauthorized select agent material. While preparing for an inspection of the Rocky Mountain Laboratories[22] in October 2011, the lead DSAT (Division of Select Agents and Toxins) inspector identified publications that indicated a NIH researcher may have conducted experiments using antibiotic resistant *Yersinia pestis* (plague).[23] After further review, DSAT determined that the NIH researcher did conduct these experiments, and failed to comply with the FSAP in 2007 when he received an unauthorized transfer of the *Y. pestis* without obtaining prior approval from DSAT. This matter was

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[16] Letter from Hon. Dr. Francis Collins, Director, NIH, to Hon. Fred Upton, Chairman, H. Comm. on Energy & Commerce (Sept. 17, 2014).
[17] *Id.*
[18] *Id.*
[19] NIH, Select Agent Investigative Report, Findings, Actions, Bethesda, MD, (June 5, 2012).
[20] *Id.*
[21] *Id.*
[22] Rocky Mountain Laboratories is an NIH facility located in Hamilton, Montana.
[23] Letter from Robin Weyant, Director, CDC Division of Select Agents and Toxins, to Tony Maida, Senior Counsel, HHS-OIG, (December 9, 2011).

referred to HHS-OIG on December 9, 2011, from DSAT.[24] After this discovery, the NIH retrained all Select Agent PIs by the NIH SAP, and it was during this retraining effort that the two NIH PIs self-disclosed possession of the *B. anthracis.*

After NIH reported the discovery of anthrax in 2012, DSAT conducted an onsite visit of NIH. In a letter addressed to the NIH RO, DSAT informed NIH that it "[h]ad significant concerns regarding the compliance of the NIH with the requirements of 42 CFR Part 73 Section 73.8 of the select agent regulations."[25] The following concerns were identified by DSAT's site visit:

- NIH failed to ensure that the biosafety and containment procedures were sufficient to contain the select agents;
- NIH failed to implement provisions of the NIH security plan to safeguard select agents against unauthorized access, theft, loss, or release in violation of section 11of the select agent regulations;
- NIH conducted work with the select agents that had not been approved by DSAT and failed to restrict access to select agents to personnel approved by HHS;
- The RO failed to ensure compliance with the select agent regulations during annual inspections of select agent registered laboratories; and
- The RO failed to ensure an accurate, current inventory for each select agent held in long-term storage.

As a result of these observations, DSAT asked NIH to "[s]how cause why the registration of the NIH (Registration #C20110919-1265) should not be suspended or revoked."[26] DSAT ultimately placed NIH on a Performance Improvement Plan Program (PIPP).[27]

The FDA was also involved in the 2012 anthrax discovery because six vials of A-34 (a strain of *Bacillus anthracis*) was found in an FDA laboratory freezer in Building 29A on the NIH campus in Bethesda, Maryland.[28] After this discovery, all PIs on NIH's campus completed written attestation forms, attesting to the fact that each PI surveyed their laboratory spaces for select agent materials and that none were found. FDA staff on campus also submitted attestation forms.[29] The Committee interviewed the FDA PI that worked in Building 29A on NIH's campus, and he explained that he only checked his own materials for select agents, and did not check other materials. As a result of FDA's failure to require researchers to conduct inventories of all items maintain in shared spaces, the discovery of the smallpox vials was delayed until 2014.

B. 2009 – NIH Inventory Discrepancy

A 2009 HHS OIG audit report about NIH's compliance with Federal select agent regulations reported concerns about inventory management stemming from an unexplained inventory discrepancy. The discrepancy stemmed from the NIH's handling of sealed envelopes, unopened since 1960, containing historical specimen select agents. The select agents included plague and Burkholderia. Apparently, the

[24] *Id.*
[25] Letter from Robbin Weyant, Director, CDC Division of Select Agents and Toxins, to Deborah Wilson, Responsible Official, NIH, (June 4, 2012).
[26] *Id.*
[27] *Id*.
[28] Letter from Thomas Kraus, Associate Commissioner for Legislation, FDA to the Hon. Fred Upton, Chairman, H. Comm. on Energy and Commerce (Sept. 18, 2014).
[29] *Id.*

NIH clinical laboratory registered the sealed envelopes in the Federal Select Agent Program around 2002 or 2003 based on the labels on the envelopes, but did not actually open the envelopes to inspect the materials within. Because of a flood in 2007, these envelopes were transferred to the NIH OSH office (the office responsible for overseeing NIH compliance with select agent regulations), and were re-registered with FSAP, but again without opening the envelopes. In 2008, while preparing for an HHS OIG on-site audit, a lab in the NIH clinical laboratory performed a hand count inventory and opened the sealed envelopes. One of the envelopes contained seven more vials of the select agent Burkholderia than was listed.[30]

Interviews with NIH staff advised that the materials were registered using information on the envelopes' labels. This practice raises several concerns. Since the envelope was not opened until at least five years after registration, the NIH could not and did not confirm the number of vials and materials on the label to assure the accuracy of the registration information submitted to CDC both in 2003 and in 2007. Further, without opening the envelopes, the NIH could not and did not ensure that a breach did not occur, or that the select agents were secured properly in the vials.

The NIH also told the OIG that envelopes are considered acceptable containers for storage,[31] and cited 42 CFR 73.17 several times. [32] Not only was the citation provided by NIH incorrect, but even the correct citation did not show that envelopes are acceptable for storage under the FSAP. The NIH did not report any information to the OIG about the circumstances surrounding the envelopes containing the select agents. At the time of the writing of this memorandum, the NIH had not provided an explanation of how envelopes could qualify as containers for storing select agents.

IV. Findings

Question: With respect to the vials of smallpox virus discovered in July 2014, did the NIH and the FDA fail to account for all select agent materials in its possession as required?

Finding: Yes. Both the NIH and FDA failed to include the smallpox discovered in Building 29A in the registration application to the Federal Select Agent Program in 2003.

Discussion:

Per 42 U.S.C. § 262a, the NIH is responsible for ensuring compliance with the Federal select agent regulations for all select agent materials in its possession.[33] Thus, even if the FDA was using NIH space, NIH's RO was responsible for the space.[34]

The CDC reported to the Committee that NIH submitted the required "notification of possession" of select agent forms[35] to HHS in 2002, but did not indicate possession of any smallpox virus.

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[30] HHS-OIG, "Review of the National Institutes of Health Bethesda, Maryland, Laboratories' Compliance with Select Agent Regulations," A-03-09-00350, December 2009.
[31] *Id.*
[32] Email from Anne Tatem, NIH to Committee staff, April 13, 2016.
[33] Letter from Dr. Thomas Frieden, Director, CDC to the Hon. Fred Upton, Chairman, H. Comm. on Energy and Commerce (August 22, 2014).
[34] *Id*. at 6.
[35] Pursuant to 42 CFR §73.9 (a)(6), the Responsible Official required to register select agents must ensure that annual inspections are conducted for each laboratory where select agents or toxins are stored or used in order to determine compliance with these requirements. The results of each inspection must be documented, and any deficiencies identified during an inspection must be

Notably, the form explicitly listed Variola major (smallpox virus) as a select agent requiring notification. The registration application submitted to the Federal Select Agent Program by NIH, as required under the select agent regulations, likewise did not acknowledge possession of Variola viruses.

Further, the CDC reported that neither the FDA nor the NIH identified the possession of smallpox.[36] While NIH registered the building with the Federal Select Agent Program, it failed to register the space where the vials were found and the vials themselves. The individual who served as NIH's Responsible Official in 2003, the Director of the NIH Division of Occupational Health and Safety, is still the current NIH RO.

The NIH reported that it had no records of the transfer of smallpox and other pathogen samples when the office that had custody over the vials was transferred from NIH to the FDA in 1972.[37] During a November 21, 2014 bipartisan Committee staff briefing, the NIH RO acknowledged that the agency did not comply with Federal select agent regulations because it did not identify the smallpox vials.

Question: **Was the smallpox incident the only occasion on which the NIH apparently violated the Federal select agent regulations for lack of accountability and improper storage of a previously unidentified select agent?**

Finding: No. The NIH previously failed to account for vials of *Bacillus anthracis* spores in an unregistered space in February 2012.

Discussion:

As discussed above, with respect to the 2012 discovery of *B. anthracis* spores, the Committee's investigation determined that the discovery of unreported, unregistered anthrax during a laboratory inspection resulted from two principal investigators self-disclosing to the NIH Select Agent Program on January 26, 2012, during a Select Agent Program retraining, about their unauthorized work involving antibiotic resistant *Bacillus anthracis*. The Committee further learned that the Select Agent retraining effort in January 2012 occurred because of a previous discovery of unauthorized select agent material.

Recent interviews with NIH staff acknowledged that the 2012 laboratory searches only searched registered spaces for anthrax because NIH believed it had no reason to suspect that there was inappropriate storage of other materials. Yet, NIH learned about the unreported, unregistered anthrax after its discovery the prior year that an NIH researcher received an unauthorized transfer of plague. Had NIH undertaken a more extensive review in response to these problems with two different select agents, the smallpox vials could have been discovered years earlier.

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corrected. In addition, under 42 CFR §73.9 (c)(1), the Responsible Official must immediately report the identification and final disposition of certain enumerated select agents or toxins, including the smallpox virus.

[36] *Id.* On July 12, 2002, the CDC published a notice stating that facilities should complete a "notification of possession" form by September 10, 2002, based on an inventory of its facility and consulting with others (e.g., principal investigators), as necessary, to obtain information required for the form. The "notification of possession" form was to be submitted to HHS under the Public Health Security and Bioterrorism Act. In addition, the HHS Federal select agent regulation (42 CFR § Part 73.9 (c)(1)) became effective on February 7, 2003, and required the registration of the possession, use, and transfer of select agents and toxins, including Variola major and Variola minor viruses.

[37] Letter from Hon. Dr. Francis Collins, Director, NIH, to Hon. Fred Upton, Chairman, H. Comm. on Energy & Commerce (Sept. 17, 2014).

Question: **Prior to the July 2014 discovery of undeclared smallpox, had the NIH previously engaged in checking inventories or conducting surveys for undeclared and unregistered Federal select agents, including cold storage rooms?**

Finding: Yes. These efforts, however, assumed that any potential select agents would be attributed to a researcher and did not include searches or surveys to cover select agents that were not "owned" or under the control by any current researcher.

Discussion:

After the 2012 anthrax discovery, the NIH initiated a search of all laboratories known to work with any form of anthrax, regulated or unregulated, to ensure that no further anthrax was stored inappropriately. This inspection found regulated anthrax in three other unregistered locations on campus, including in Building 29A, where the smallpox vials were ultimately discovered.[38] The NIH focused only on anthrax despite learning of an unauthorized transfer of plague by an NIH researcher in 2007 the year before.

Notably, the NIH did not engage in any effort to account for materials in all spaces in NIH laboratories—searches and inventory checks were limited to researchers, materials, or spaces already registered to the FSAP. For example, while the lab sweep focused on anthrax vials, all NIH Principal Investigators and FDA PIs in NIH buildings registered with FSAP had to sign written attestations that they had no other unregistered select agents. Had the NIH focused its lab sweep on all select agents or had the NIH investigated the possibility of unregistered locations improperly storing select agents, it may have discovered the 327 vials of dangerous pathogens, including smallpox, years earlier. In an April 8, 2016 meeting with Committee staff, the NIH Principal Deputy Director acknowledged that the scope of NIH's investigation was flawed because it assumed that the universe for possible improperly stored select agents would be limited to researchers and locations already registered in the Federal select agent program.

Question: **Did the NIH inspect the cold storage room containing the smallpox vials, and did the scope of these inspections include issues that related to the cardboard boxes containing the smallpox vials?**

Finding: Yes. The NIH conducted annual inspections of the cold storage room in question. The smallpox vials were stored in cardboard boxes in the cold room. The NIH's safety inspection program drew attention to the presence of cardboard storage in the very room in which the smallpox vials were ultimately discovered. The NIH safety survey used from 2011 to 2013 included a checklist to confirm that there was no cardboard storage in the cold room. During two 2011 inspections, NIH safety inspectors found cardboard in the cold room, and one of the inspectors wrote "remove all cardboard from the cold storage room." In 2012, the NIH inspectors returned and reported no cardboard in the cold room. Contradicting her earlier interview with Committee staff, the NIH RO told the Washington Post that inspectors were not actually concerned about cardboard boxes on shelves, the preponderance of evidence from documents and interviews shows the concern over cardboard mold in Building 29A cold rooms at that time was very broad and included cardboard sitting on shelves.

[38] *Id.*

Discussion:

Documents produced by NIH to the Committee show that NIH safety inspectors inspected cold storage room 3C16 as part of NIH inspections of nearby FDA labs.[39] Building 29A, which contains cold storage room 3C16, was built in 1968. In an interview with FDA staff that worked in room 3C16, staff described the building as "quite moldy" and mentioned that the cold room failed on a regular basis. The temperature in the cold room warmed to almost room temperature at times, and an FDA PI confirmed the rooms had contamination issues due to mold growth.

The NIH conducted two different safety inspections on October 11, 2011, both of which indicated the presence of cardboard storage in cold room 3C16. The first inspection completed on October 21, 2011, was for the FDA laboratory located in Building 29A, Room 3C22 (a lab on the 3rd floor C corridor permitted access to the cold storage room 3C16). The NIH inspector wrote the following comment regarding the cold room: "Please remove all cardboard from the cold room."[40] The second inspection, conducted by a different NIH inspector, also found cardboard in the cold storage room. This inspection was conducted for the laboratory located in Building 29A, Room 3C12. The NIH inspector checked "No" on "No cardboard storage" in the cold room, indicating the presence of cardboard in the cold storage room. The same PI supervised both of these labs.

In May 2015, the NIH RO told *The Washington Post* that the removal of cardboard in cold room storage referred to "Cardboard that is abandoned on floors, or in wet piles."[41] The NIH RO further remarked that "it has nothing to do with cardboard boxes on shelves in which research materials may be stored."[42] The NIH RO did not provide this interpretation to Committee staff in November 2014 when the NIH safety surveys of the cold room and cardboard storage were specifically discussed. The NIH RO did not correct or question Committee staff's view that NIH inspectors were looking at all cardboard generally in cold storage rooms, not certain categories of cardboard. These statements are also inconsistent with the Committee's recent interviews with NIH and FDA staff. In these interviews, NIH and FDA staff confirmed that the purpose of removing cardboard boxes in the storage room was to prevent mold growth. NIH and FDA staff explained that comments directing the removal of cardboard were not limited to cardboard only on floors or in wet piles, as the NIH RO stated in *The Washington Post* article. NIH and FDA staff further explained that while cardboard on the floor or wet cardboard posed the greatest risk for mold, it was an ideal best practice and recommendation to remove all cardboard for mold growth prevention. Finally, multiple safety surveys for Building 29A showed that in 2011, NIH inspectors were requesting removal of all cardboard boxes from cold rooms and in some cases specifically requesting that the cardboard boxes be replaced with plastic bins. This would be consistent with the reported maintenance problems with the aging Building 29A facility, multiple closures of cold storage rooms in Building 29A because of mold growth, four to five failures a year of the cold storage room in question as told by the FDA researcher, and the more hard-line approach toward cardboard in cold rooms that occurred in the 2011 NIH inspections in response to cold room problems in Building 29A.

The Committee also learned that each NIH campus has different safety protocols and procedures. For example, the National Cancer Institute-Frederick Fact Sheet, "Biosafety Technical Bulletin: Cold Rooms and Mold," dated November 2011, states that "[s]ince cold rooms are typically shared spaces, an

[39] *Id*.
[40] A subsequent 2012 NIH inspection confirmed that the cold room associated with the 3C22 lab was the cold storage room 3C16. Previous NIH inspections of this lab indicated that the "cold room storage" category was not applicable to this lab.
[41] Lena Sun, *House Panel Seeks Expanded GAO Review of Smallpox Incident at NIH*, WASH. POST (May 19, 2015).
[42] *Id*.

established protocol should be adopted by all users to reduce the chance of mold growth in the space. At a minimum, . . . DO NOT store cardboard, . . . in cold rooms."[43] However, other NIH campuses did not implement similar standards in their safety policies. The Committee questions whether NIH should have consistent safety and policy standards across their campuses. If so, under what circumstances would it be appropriate for campuses to have different policies?

Since the 2014 smallpox discovery, the NIH has recently revised their safety inspection form. The new form requires inspectors to limit its search of cardboard in cold room storage if the cardboard is, "free of unused, discarded, or damaged." This raises the question of whether future inspections will properly detect mold growth of cardboard inside boxes, since new inspections will be limited to external factors.

Question: Was there a previous instance of questionable NIH handling of unopened historical collections of select agents?

Finding: Yes. Both the laboratory at the NIH Clinical Center and the NIH Safety Office registered materials contained in sealed envelopes in the FSAP that were labeled as containing various select agents, including plague, without opening up the envelopes to verify the contents and the amounts.

Discussion:

As described above, a 2009 HHS OIG audit report about NIH's compliance with Federal select agent regulations reported concerns about inventory management stemming from an unexplained inventory discrepancy in a historical collection of specimens, including select agents, contained in sealed envelopes and unopened between 1960 and 2008.

The Committee is concerned about NIH's registration of the select agents contained in the sealed envelopes based only on the labels of the envelopes, and without confirming the actual pathogens contained within. Since the envelope was not opened until at least five years after registration, the NIH could not and did not confirm the number of vials and materials on the label to assure the accuracy of the registration information submitted to CDC both in 2003 and in 2007. Further, without opening the envelopes, the NIH could not and did not ensure that a breach did not occur, or that the select agents were secured properly in the vials. The Committee is further concerned about the use of envelopes as acceptable containers for the storage for select agents. Not only was the citation provided by NIH incorrect, but even the correct citation did not support NIH's assertion that envelopes are acceptable for storage under the FSAP. The NIH did not report any information to the OIG about the circumstances surrounding the envelopes containing the select agents. At the time of the writing of this memorandum, the NIH had not provided an explanation of how envelopes could qualify as containers for storing select agents.

The NIH has stated that "it is routine in the conduct of infectious disease or vaccine research and for quality control purposes to maintain collections of pathogens in laboratories. The maintenance of pathogen collections by laboratory is a common practice."[44] Given this practice, historical collections were known to NIH safety officials and subject to inventory control and Federal select agent regulation, where applicable. At other departments, such as the Department of Defense, there were written policies

[43] NCI, Frederick Campus, Biosafety Technical Bulletin, November 2011.
[44] Letter from Hon. Dr. Francis Collins, Director, NIH, to Hon. Fred Upton, Chairman, H. Comm. on Energy & Commerce (Sept. 17, 2014).

governing the accountability of abandoned or remnant research materials or materials such as historical collections without identifiable ownership. Had the NIH undertaken a search for other historical collections when it found and registered this historical collection in 2002 or 2003, the agency could have discovered the smallpox vials contained in another historical collection over a decade earlier.

Question: Did FDA have sufficient policies and protocols in place in 2014 to ensure safety in its laboratories?

Finding: No. FDA policies and protocols in place at the time did not ensure safety in its laboratories. For example, FDA did not require researchers to conduct inventories of all items maintained in storage rooms. Further, FDA did not enforce relevant policies that it did have in place at the time. These insufficient and unclear policies, in part, delayed the discovery of the smallpox vials.

Discussion:

The FDA acknowledged to the Committee its responsibility for complying with applicable Federal requirements governing the possession, use, and transfer of all select agents stored in FDA lab facilities on the NIH campus.[45] FDA explained its failure to account for all select agent material:

> Because FDA's internal procedures did not clearly assign responsibility for inventorying the contents of common cold storage areas in Building 29A, the vials were not discovered until July 1, 2014, when a thorough search was conducted in preparation for the relocation of FDA's Building 29A laboratories from Bethesda to FDA's main campus in Silver Spring, Maryland.[46]

The Committee interviewed the FDA PI who found the smallpox vials, and he confirmed that the agency did not implement a formal inventory protocol until 2014—after the discovery of the smallpox vials. The FDA PI also stated to the Committee that, prior to 2014, PIs managed their inventory by keeping a "running list" of materials in their possession.

The Committee asked the FDA about the inventory control responsibilities for the cold storage room. The FDA responded that it had no inventory control responsibilities for this room because "the cold storage room, 3C16, is not part of a custodial area since there was not any accountable government property stored in this space . . . . Accountable property is defined as computers and all pieces of equipment with a value of more than $5,000."[47] Furthermore, when the Committee asked the FDA to identify the cold storage property custodian, the FDA identified "[n]o one, for the reasons described above. There was a Point of Contact who had limited responsibilities with respect to the cold room. These limited responsibilities did not include maintaining an inventory of the contents of the cold room."[48]

The Committee also learned that while the FDA had a policy specifically for Cold Rooms, no one held staff accountable for complying with policy. FDA's Cold Room Policy issued in 2011 required that "[a]ll materials in the cold room should be properly labeled, including owner's name and work phone

[45] Letter from Thomas Kraus, Associate Commissioner for Legislation, FDA to the Hon. Fred Upton, Chairman, H. Comm. on Energy and Commerce (Sept. 18, 2014).
[46] *Id*.
[47] Email from FDA counsel, to Committee staff (Dec. 11, 2014).
[48] *Id.*

number."[49] The boxes containing smallpox vials were unlabeled despite this policy issuance, and FDA never at any time prior to 2014, required that an individual be identified as a contact for its contents. The Committee's interviews with FDA staff confirmed that each PI who used the cold storage room was responsible for taking inventory of his or her own specimens. Interviews with FDA staff also confirmed that FDA had an unwritten policy on handling the abandonment or transfer of research materials.

The Committee has learned about recent changes to FDA's safety and oversight for laboratories. Recently, the FDA hired a Director for the Office of Laboratory Science and Safety. FDA has communicated their intentions to assign a Responsible Official to each cold storage room, and to implement an electronic inventory mechanism that allows researchers to upload materials in real-time. The inventory documentation will identify a description and quantity of the materials, where the materials are located, and who is responsible for the materials. In addition, FDA has informed the Committee that they plan to implement an official policy on the transfer or abandonment of materials. Furthermore, FDA relayed that it plans to hire staff for the Office of Laboratory Science and Safety to oversee these forthcoming implications. The Committee acknowledges that these new procedures sound promising; however, it is unclear when the Office for Laboratory Safety will expand due to budget.

Question: **Are there concerns with CDC's oversight of NIH compliance with the Federal Select Agent Program?**

Finding: Yes. The CDC's Division of Select Agents and Toxins did not examine NIH's response to earlier incidents upon discovering new violations, and, until recently, narrowly construed requirements so that reports to Congress on notifications, thefts, losses, or releases of select agents did not include discoveries of select agents not previously accounted for and reported to the Federal Select Agent Program.

Discussion:

The CDC's Division of Select Agents and Toxins is responsible for assessing FSAP violations. DSAT has the authority to deny, suspend, or revoke an entity's registration, and may require an entity to enter into a Performance Improvement Plan. In July 2011, HHS OIG audited FSAP compliance, specifically evaluating DSAT. OIG found that DSAT did not effectively monitor and enforce certain FSAP regulatory provisions. OIG also found a high incidence of access to select agents by unapproved persons during select agent transfers. The CDC concurred with OIG's recommendations for improvements to its FSAP oversight; however, the Committee continues to observe inadequacies with the DSAT enforcement.

On September 8, 2014, the CDC DSAT referred NIH's 2014 discovery of smallpox to the HHS-OIG for potential FSAP violations. In the referral letter, the CDC DSAT mentions that the 2014 smallpox referral "supplements the information provided in April 2012 of NIH's discovery of *Bacillus anthracis* in areas not listed on NIH registration application."[50] Although the CDC DSAT recognized a connection between the 2012 and 2014 incidents, there was no further examination of why previous efforts, such as past performance improvement plans, were ineffective at detecting unregistered vials of smallpox. Nor is there any evidence that CDC asked NIH for a stronger performance improvement plan in light of the smallpox discovery.

[49] FDA,CBER Cold Room Policy (2011).
[50] Letter from Robbin Weyant, Director, CDC Division of Select Agents & Toxins, to David Blank, Senior Counsel, HHS-OIG, (Sept. 8, 2014).

After the 2014 NIH laboratory clean sweeps, DSAT learned that the sweep identified additional select agent material.[51] As a result, DSAT Director instructed staff to "prepare a package for consideration of compliance penalties by the HHS IG. Although NIH is being admirably responsive and transparent in their reporting these discoveries, the retention of multiple samples if Tier 1 BSAT outside of secure registered space is a serious compliance matter."[52] The Committee has learned that DSAT took no additional action, despite DSAT explicitly stating that NIH's FSAP violations were a serious compliance matter. DSAT did not revoke or suspend NIH's registration in the FSAP. The Committee is disappointed in the lack of enforcement by DSAT.

Lastly, for more than a decade, the CDC failed to implement a policy for the reporting of discovered select agents and toxins in unregistered areas. Prior to 2015, the CDC's "Form 3" required entities to report only instances of theft, loss, and release of a select agent or toxin. The form did not include discoveries of unregistered select agent materials since the inception of the FSAP program. In a response to the Committee regarding the use of the Form, CDC explained that "NIH did not submit a Form 3 to the Federal Select Agent Program (FSAP) reporting the discovery of the vials as a loss, and FSAP did not treat the discovery of these vials as a loss in the 2014 Annual Report to Congress."[53] As Congress relies on the Form 3 to identify the number of inadvertent lapses in the FSAP, the CDC's failure to report unregistered discoveries is misleading.

Question: Did the Office of Inspector General take timely action with respect to the CDC referrals concerning the NIH?

Finding: No. After receiving the CDC referrals concerning NIH's FSAP violations, OIG took years to resolve the referrals.

Discussion:

HHS receives FSAP referrals from the CDC DSAT if an investigation determines that a civil violation may have occurred. Once HHS receives the referral, the Office of Inspector General evaluates the case and, if OIG concludes there is a violation, OIG determines the appropriate disposition of the case. OIG has three options to resolve a DSAT referral: (1) imposing a Civil Monetary Penalty (CMP), (2) issue a Notice of Violation letter, or (3) close the case. During the Committee's July 2015 hearing on anthrax shipments, Chief Counsel to the Inspector General for HHS OIG testified that the OIG has not imposed a CMP on a Federal entity for FSAP referral violations.

DSAT referred a total of four FSAP violations on NIH to HHS OIG, with the oldest referral dating to 2011. Until this month, all four NIH referrals had remained open by OIG. OIG recently informed the Committee and CDC that it plans to close all four referrals without imposing any monetary fines. Officials at NIH and FDA informed Committee staff that the HHS OIG's open investigations of the DSAT referrals was a factor in each agency's decision to refrain from conducting any internal and retrospective review on the systemic factors contributing to the 2014 smallpox incident. The HHS OIG's recent reaffirmation of an earlier decision not to impose civil monetary fines on Federal laboratories as a practical matter now limits enforcement over civil violations to the CDC. Those potential CDC enforcement actions are limited to performance improvement plans, or revocation/suspension of Federal select agent registration.

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[51] Email from Robbin Weyant, Director, CDC Division of Select Agents & Toxins, to Sonja Rasmussen, Joanne Andreadis, & Roberto Ruiz, CDC Division of Select Agents & Toxins (Aug. 20, 2014).
[52] *Id.*
[53] Email from Barbara Rogers, CDC, to Committee staff (April 8, 2016).

V. Conclusion

The majority Committee staff's preliminary investigation uncovered several issues related to the discovery of the smallpox vials that require further investigation by the HHS agencies. These issues include: the failure to account for regulated select agents; the failure to conduct comprehensive inventory of all select agent material; and the failure to restrict unauthorized access to select agents. Concerns are also raised about current FSAP enforcement as applied to Federal laboratories since neither the FDA nor the NIH received sanctions or penalties from the Office of Investigations for FSAP violations.

To date, neither the FDA nor NIH has conducted an internal investigation (along the lines of CDC and Army internal investigations) on the events leading to the discovery of smallpox. While senior officials from the NIH and FDA have recently indicated a willingness to conduct an internal review, neither has informed the Committee that they are, in fact, initiating such a review. This much needed internal review is in addition to the policy changes and oversight efforts currently under review and implementation at HHS agencies.

Dr. Lawrence Tabak, the Principal Deputy Director for the National Institutes of Health, and Dr. Segaran Pillai, Director of the Office of Laboratory Science and Safety for the FDA, will be testifying at the Committee's April 20 hearing. Members will have an opportunity to question these witnesses about issues arising from the information presented in this memorandum.