

**Appendix E Supplement**

**CDC-FBI Investigation/Report**



**TO:** National Institutes of Health  
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Bethesda, MD 20892  
FAX: (301) 480-0701

**FROM:** Centers for Disease Control and Prevention, Division of Select Agents and Toxins

**DATE:** August 8, 2014

**RE:** Joint CDC and FBI Investigation of Vials labeled "Variola" and other Vials Discovered on the NIH Bethesda, MD Campus

Pursuant to the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, the United States Department of Health and Human Services (HHS) has established regulatory requirements for the possession, use, and transfer of biological agents and toxins that have the potential to pose a severe threat to public health and safety. These requirements can be found at 42 CFR Part 73. The Centers for Disease Control and Prevention's (CDC) Division of Select Agents and Toxins (DSAT) inspects entities to evaluate whether they meet the regulatory requirements set forth in 42 CFR Part 73. See 42 CFR § 73.18. The above referenced regulations and supporting guidance information may be found at <http://www.selectagents.gov/>.

#### **Background**

On July 1, 2014,

\_\_\_\_\_ for the NIH Bethesda, MD campus registered entity notified the CDC DSAT of the discovery of vials possibly containing Variola virus (the material) on the NIH Bethesda campus.

In response to this notification, CDC DSAT and the Federal Bureau of Investigation (FBI) conducted a joint investigation at the NIH Bethesda, MD campus, from July 7 - 9, 2014, to gather the facts regarding the discovery of the material, how the material was secured upon discovery, the security environment the material was in prior to its discovery, and what actions the NIH Bethesda, MD campus is, or will be, taking to prevent any future incidents of this type.

The following CDC DSAT personnel participated in the investigation (CDC DSAT Investigation Team):

\_\_\_\_\_

The following personnel from the HHS Office of General Counsel participated in the investigation:

[REDACTED]

[REDACTED]

**The following FBI personnel participated in the investigation:**

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**The following Food and Drug Administration (FDA) and NIH personnel were present at some point during the investigation:**

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**The following personnel from the CDC Division of High-Consequence Pathogens and Pathology assisted in the laboratory investigation:**

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**The CDC DSAT investigation team was on the NIH Bethesda, MD campus at 10 a.m. on July 7, 2014 and started a joint investigation of the incident with the FBI. In addition, on July 7, personnel from the CDC Division of High-Consequence Pathogens and Pathology assisted the FBI in reviewing the labels on the vials, establishing a preliminary inventory of the vials, and the transfer of sixteen of the vials to the CDC in Atlanta, GA. The CDC DSAT and FBI investigation continued on July 8. On July 9, 2014, one member of the CDC DSAT team remained onsite with FBI personnel to witness the destruction of some of the vials and the transfer of the remainder of the vials to the FBI for transport to the U.S. Department of Homeland Security's National Bioforensic Analysis Center.**

**During the CDC DSAT and FBI joint investigation, seven FDA and NIH staff were interviewed (see Appendix A), including all four FDA and NIH personnel that were associated with the discovery or**

subsequent handling of the material. Records were obtained that included access records to building 13 room 3W84B, where the material was secured upon discovery.

The observations and findings during the joint CDC and FBI inspection are provided below.

### Description of the Event

Based on interviews with FDA and NIH personnel associated with the discovery or subsequent handling of the material (Appendix A), events transpired on July 1, 2014 as follows (a graphical time line of these events is provided as Appendix B):

- Between approximately 11:30 a.m. and 12:30 p.m. an FDA investigator, [redacted] is in cold storage room 3C16 in building 29A, determining what pieces of equipment will be moved to the FDA White Oak Facility in Silver Spring, MD (photos of the cold room, a room generally held at 4° C and used for extended storage of materials or equipment requiring refrigeration, are provided as Appendix D).
- At approximately 12:30 p.m., [redacted] investigates the contents of 12 brown cardboard boxes located on a shelf in the back left corner of the cold room (photos are provided as Appendix D). In the first box opened, he sees, among the other glass vials with typed labels, a vial of lyophilized material bearing the typed label: "variola." [redacted] immediately closes the box, exits the cold room, and proceeds to laboratory 3C22 to wash his hands.
- At approximately 1:00 p.m., [redacted] goes to the office of a second FDA investigator, [redacted] a virologist, and describes to him the aforementioned events and discovery of the vial labeled "variola."
- At approximately 1:00 p.m., [redacted] return to cold storage room 3C16. They reopen the box identified by [redacted] and further examine the contents, identifying a second vial labeled "variola."
- Between approximately 1:00 p.m. and 1:30 p.m., [redacted] look through additional boxes, finding vials with labels such as "Q-fever," "rickettsia," and an additional vial labeled "variola."
- At approximately 1:30 p.m., [redacted] finish their investigation of the boxes, leave them in the cold room, exit to wash their hands in nearby laboratory 3C22, and go to the office of [redacted] supervisor, [redacted] was not in her office. [redacted] emails her indicating that he would like to have a discussion upon her return.
- Between 4:30 p.m. and 5:00 p.m., [redacted] emails [redacted] indicating that she has returned to her office and is available to talk.
- At approximately 5:00 p.m., [redacted] goes to the office of [redacted] the two then proceed to [redacted] office and inform her of the aforementioned events leading to the discovery of the vials labeled "variola."
- [redacted] informs [redacted] that she would be contacting the director of the NIH Division of Occupational Health and Safety (DOHS), [redacted] return to their offices.
- At approximately 5:30 p.m. [redacted] contacts [redacted] tells her to bring the material to the DOHS office on the third floor of building 13.
- At approximately 5:35 p.m. [redacted] contacts [redacted] and the two of them meet in the cold storage room 3C16. They do not open any boxes, and wearing a lab coat and gloves, place all 12 boxes into a larger cardboard box. The used lab coats and gloves are also placed into the larger box with the 12 smaller boxes. The larger box is sealed with clear packaging tape, and [redacted] alone hand-carries the material to the NIH DOHS office on the 3<sup>rd</sup> floor of building 13. An aerial view of the route taken between building 29A and building 13 is provided as Appendix C.

- At approximately 5:50 p.m., \_\_\_\_\_ arrives and meets \_\_\_\_\_ at the NIH DOHS office. \_\_\_\_\_ initiates a chain of custody form to document the transfer of the material from FDA to NIH. \_\_\_\_\_ and \_\_\_\_\_ proceed to the BSL2 laboratory, building 13 room 3W84. \_\_\_\_\_ disarms and opens the door to room 3W84. \_\_\_\_\_ hands over the material to \_\_\_\_\_ who takes the material into 3W84. \_\_\_\_\_ remains outside of 3W84, but watches through the window as \_\_\_\_\_ disarms and enters RSL3 laboratory, 3W84B, and places the material in the biosafety cabinet within 3W84B. \_\_\_\_\_ walks back to her office in the building 29 complex and notifies her supervisor,
- Between 6:00 p.m. and 6:08 p.m. \_\_\_\_\_ tries three times to get in contact with the FBI. The FBI makes contact with \_\_\_\_\_ at 6:28 p.m.
- At 6:35 p.m. \_\_\_\_\_ calls and notifies the CDC DSAT director.

According to access logs provided by NIH, no personnel accessed BSL3 lab 3W84B after 5:51 p.m. July 1, 2014 until 10:54 a.m. July 7, 2014 when the joint CDC Division of High-Consequence Pathogens and Pathology and the FBI team started the photo documentation and preliminary inventory of the vials.

### **Description of the Security Environment of the Material upon Discovery and Prior to Its Transfer to FBI Custody**

At the time of its discovery, the material was in an unsecure, shared cold storage room, 3C16, on the third floor of building 29A. Once discovered, the material was packaged in a larger cardboard box and transported to a BSL3 laboratory in building 13, room 3W84B.

#### Security of Campus

- Buildings 29, 29A, and 29B (building 29 complex) and building 13 reside on a closed campus. The campus is protected by a perimeter fence, surveillance cameras, guards at the entrances, as well as roving security.
- Security is managed by a Security Operations Center which monitors alarms and directs response (NIH Division of Police).

#### Security of Building 29 Complex

- The building 29 complex consists of 3 buildings, 29, 29A, and 29B, linked by common hallways.
- There are 13 exterior doors to the building 29 complex (4 have card readers and guards; the remaining doors are keyed).
- Access to the building 29 complex is limited to FDA, NIH, and HHS employees with access to the NIH campus.
- With the exception of laboratory 3A03 in building 29A, which is registered with the Federal Select Agent Program<sup>1</sup> and has access controls administered by NIH, access to all other areas within the building 29 complex is administered by the FDA.
- There are four video cameras on the outside of the building. The video cameras do not completely cover the building perimeter.

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<sup>1</sup> The Federal Select Agent Program, a joint effort of the CDC's DSAT and the Animal and Plant Health Inspection Services' Agriculture Select Agent Services, has regulatory oversight of the possession, use and transfer of biological select agents and toxins, which have the potential to pose a severe threat to public, animal or plant health or to animal or plant products.

- During business hours there are five guards on duty (four at access points and one roving guard); after business hours there are three guards on duty (two at access points and one roving guard).

### Security of Cold Room 3C16

- 3C16 is located on the 3<sup>rd</sup> floor of building 29A.
- The cold room is accessed from a common hallway, across from a suite of laboratories.
- The space is currently shared between the laboratories of two FDA investigators and [redacted]. They are from different FDA divisions. [redacted] and [redacted] did not know who may have stored material in this room before 1992. [redacted] thought the material was in the room before he began using the room in the 1990s.
- At the time of the discovery, the room was not locked and there is no indication that it has been locked in the past.
- There is no means to determine who may have entered the room (e.g. card key readers, access logs, or video cameras).
- There was no means to determine who was responsible for the storage area or who owned material inside room 3C16.

### Security of laboratory 3W84B in Building 13

- During work hours when the building is occupied, there are two secured doors.
- After work hours, the main points of entry to building and an additional door are automatically locked.
- Access to the BSL3 laboratory is restricted by three different electronic mechanisms and the room is monitored by an intrusion detection system. The BSL3 laboratory is within a BSL2 laboratory, room 3W84.
- Personnel who had access to the BSL3 laboratory (3W84B), after a Security Risk Assessment previously conducted by the FBI, have been approved by the Federal Select Agent Program for access to select agents and toxins; and are enrolled in the NIH Bethesda, MD campus personnel reliability program.
- Between July 4 and 7, 2014 there were two FBI agents stationed at the access point to BSL2 laboratory 3W84.
- Three NIH and FDA personnel knew that the material found in building 29A was stored inside the building 13 BSL3 laboratory 3W84B. [redacted] both knew its location and had access. [redacted] was present when it was stored, however she stated she did not tell anyone and when asked, could not recall the room number. [redacted] did not know the storage location.
- No one entered laboratory 3W84B after 5:51 p.m., July 1, 2014 until 10:54 a.m., July 7, 2014 when the personnel from the CDC Division of High-Consequence Pathogens and Pathology and the FBI entered the room to begin their inventory of the materials contained in the box.

### **Description of Biosafety and Security Oversight for Building 29A**

Access to the building 29 complex is administered by and limited to FDA, NIH, and HHS employees with access to the NIH Bethesda campus. With the exception of laboratory 3A03 in building 29A, which is registered with the Federal Select Agent Program and has access controls administered by NIH, access to all other areas within the building 29 complex is administered by the FDA.

[redacted] indicated that as a tenant, work conducted by FDA researchers is subject to review and approval by the NIH Institutional Biosafety Committee (IBC) and must adhere to the stipulations of the IBC as well as overall NIH biosafety requirements. However [redacted] said that NIH does not

...the ... of ...

perform laboratory inspections of the FDA labs, with the exception that they do laboratory safety surveys when active work is being conducted if the laboratories are registered with the NIH Recombinant DNA Advisory Committee (RAC).

Interviews with \_\_\_\_\_ indicated that NIH is in charge of the safety oversight of the work being conducted in the building 29 complex. They indicated that, annually, people from NIH inspect their laboratories, but to their knowledge the NIH personnel have never inspected cold rooms in the building 29 complex.

When interviewing \_\_\_\_\_ for the building 29 complex, she likewise indicated that NIH manages safety for the building 29 complex. \_\_\_\_\_ indicated that in the 11 months she had worked there, she had never done a laboratory inspection or been in the 3C16 cold storage room. According to "Response to CDC Memo of July 11, 2014" the FDA biosafety specialist serves as a liaison between FDA research staff and the NIH DOHS.

We also asked who had "ownership of cold room." \_\_\_\_\_ is listed on the door as a point of contact. However, \_\_\_\_\_ indicated that there is no formal agreement or policy assigning any one person responsibility for the contents of the room. \_\_\_\_\_ indicated that the cold rooms are officially assigned to different divisions and groups. \_\_\_\_\_ echoed the sentiment that cold rooms are shared storage spaces but indicated that there is no centralized assignment of the cold room space. \_\_\_\_\_ said that people voluntarily list themselves as the contact person in case there are problems with the cold room. There was no biological hazard signage on the door.

On July 11, 2014, CDC DSAT requested that \_\_\_\_\_ provide additional information to better understand the relationship between the FDA building 29 complex and NIH, the biosafety and security responsibilities for oversight of the building 29 complex, and any additional measures that have been taken to ensure that no additional regulated materials exist on the NIH Bethesda, MD campus in areas not registered with the Federal Select Agent Program (Appendix F).

The information provided by \_\_\_\_\_ in response to the CDC DSAT request was received on July 18, 2014 and includes an update on the actions taken to ensure there is no more of this type of material in unregistered space on the NIH Bethesda campus (see below for a summary of those actions).

**Description of progress made, since July 1, 2014, in assessing the contents of cold storage rooms in buildings 29, 29A, and 29B along with other laboratory and storage areas on the NIH Bethesda, MD campus.**

On July 1, 2014, and July 8, 2014, respectively, FDA personnel and DSAT personnel separately searched cold room 3C16 where the material was discovered; with no additional material of this type being found.

\_\_\_\_\_ and \_\_\_\_\_ provided documents indicating that on July 3 and 8 they examined all other cold rooms in the building 29 complex looking for additional unassigned biological material and found none.

As of July 18, 2014, NIH and FDA created a new "attestation" document requiring FDA PIs to check their laboratory, its contents and all associated freezers, refrigerators, cold rooms, storage cabinets for select agents on the NIH Bethesda, MD campus.

Effective July 18, 2014, FDA ceased moving material from the building 29 complex to its White Oak facility until the attestation is completed by each FDA PI. This includes the materials already transferred from NIH to the FDA White Oak campus. Furthermore, before any more material is moved from the NIH

campus to the White Oak campus, FDA is requiring that the entire contents of each storage container be visually surveyed and any select agent be identified and handled in accordance with the NIH safety plan.

Effective July 18, 2014, NIH created a new "attestation" statement requiring all NIH Institutes and Centers (IC) Scientific Directors to attest, by September 30, 2014, that all IC laboratories, contents, and all associated freezers, refrigerators, cold rooms, storage cabinets had been surveyed for select agents and other potentially hazardous biological materials. All human pathogenic organisms that require BL2 level 2 containment and above, and biological toxins, venoms, or poisons will be recorded and inventoried as to location and reported to NIH/DOHS.

NIH has directed a 'clean sweep' of all NIH laboratories, clinical spaces, and offices associated with laboratories to be completed by September 30, 2014. This will include identification and labeling of material. It will also include assigning a responsible person for the material or destruction if it's not needed. Phase 2 of this plan is under development and will address policy review and revision, potential changes to the NIH Table of Penalties, and establishment of enhanced management responsibilities.

After the "clean sweep," NIH/DOHS will perform systematic compliance checks of all the laboratory spaces, all freezers and refrigerators, cold rooms, dry storage areas, etc. including review of the inventories for potentially hazardous biological materials.

For areas registered with the Federal Select Agent Program, DOHS will provide follow-up compliance checks of storage areas during annual surveys of registered laboratories (those conducting infectious disease and recombinant nucleic acid research). Safety specialists will document compliance checks.

## **Findings**

The cold room where the glass vials were found has been used by numerous investigators since at least 1992 and likely since the building was constructed in 1968. Though the room had the capability of being locked, interviewed FDA personnel indicated that the room had never been locked to their knowledge, going back to at least 1992.

There were no access logs or inventory records for any material or equipment in the cold room where the vials were found.

The material found by FDA personnel and transferred to \_\_\_\_\_ consisted of a total of 327 glass vials of lyophilized material in 12 boxes.

At least nine of the 327 vials had labels indicating that they were potentially select agents (six Variola major virus or Variola minor viruses, one Russian Spring and Summer Encephalitis virus, one Eastern Equine Encephalitis virus, and one *Coxiella burnetii*):

1. "Variola- Lee Strain, 2nd egg passage, CAM 20% in milk, 2.5cc, 11FEB47" one vial
2. "Variola- Kim Strain, 2nd egg passage, CAM 20% in milk, 2.5cc, 11FEB47" one vial
- 3 - 4. "Alastrim, CAM3, 20% suspension, 0.5cc dried, 7APR59" two vials
- 5 - 6. "Variola-Yamada, 32 egg pass, 20% CAM, susp. In H2O, 2cc, 10FEB54" two vials
7. "RSSE 45, 10%MB, 1.0cc, 1/26/57" one Vial
8. "EEE 462" one vial
9. "Q fever (Dyer strain)" one vial

One vial was labeled "RMSF." Until December 4, 2012, Rocky Mountain Spotted Fever or *Rickettsia rickettsii* was listed as a select agent.

On July 7, 2014, vials 1 - 7 along with 9 other vials that could not be identified by their labels were sent to the CDC Poxvirus and Rabies Branch BSL-4 laboratory (a total of 16 vials). One vial labeled "NOR. SPL. ANT. Lot 1 1.0ml 11/19/59" was found breached and destroyed by submersion in Microchem.

On July 9, 2014, 31 vials, four labeled "Vaccinia WR 10% IN 20% NRS 2mol pass 1.0ml 4/17/52 and 27 additional vials labeled "NOR. SPL. ANT. Lot 1 1.0ml 11/19/59" were destroyed using the autoclave in the building 13 BSL2 laboratory 3W84. The remainder of the vials, including vials 8 and 9, were moved to the U.S. Department of Homeland Security's National Bioforensic Analysis Center on July 9, 2014 (a total of 279 vials).

On July 8, 2014, the CDC Division of High-Consequence Pathogens and Pathology confirmed by using two variola-specific PCR assays that all six vials that were labeled "Variola" or "Alastrim" contained Variola virus genetic material.

On July 10, 2014, the CDC Division of High-Consequence Pathogens and Pathology confirmed that the Variola virus in at least two of the six vials was viable, therefore confirming that the material was a select agent.

The 12 boxes were marked on the outside with a series of Roman numerals and letters, IA - IH, IIA - IIC, and IIF - IIH. Based upon the numbering system, there may be at least two boxes that are not accounted for (i.e. IID and IIE). All other lettering on the outside of the boxes had been previously marked through. Although some of the marked out lettering was legible (e.g., Measles, Enders strain, Rubella, bent tip pipettes), none of the boxes contained information that identified the source of the material (e.g. PI name or organization). Photos are presented as Appendix D.

The dates on the labels on the vials ranged from the 1946 to the 1964. While the vast majority of the labels did not contain any information identifying any particular source of the material (e.g. PI name or organization), some of the labels contained possible names or potential sources (e.g. Department of Biologics Research WRAIR, WRAMC L13, Microbiological Associates Bethesda, Maryland).

Interviews with [redacted] revealed that the boxes may have been in cold room 29A/3C16 where the material was discovered since at least the early 1990's, but no one was aware of the owner or source of the material.

The location in which the material was found does not meet the requirements of the select agent regulations (42 CFR Part 73) for the possession of select agents in general and for Variola virus in particular, and there were significant vulnerabilities with access control and accountability.

After discovery, though the location in which the material was stored did not meet the specific additional requirements of the select agent regulations required for possession of Variola virus, the investigation team did not identify any significant vulnerability for the short time it was secured in the building 13 BSL3 laboratory, room 3W84B.

When moved from building 29A to building 13, the vials were not packaged and transported in a manner sufficient to prevent their release from the transport container (cardboard box) in the event of an accident, and, had 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 is not known when this breach occurred but this could have occurred during the movement on July 1, 2014 to building 13. In her interview,

indicated that she heard the vials clinking together as she transported them from building 29A to building 13.

Section 202 (a) of Public Law 107-188, the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, signed into law on June 12, 2002, directed the HHS Secretary to provide written guidance within 30 days of enactment of the bill on how facilities in possession of select agents shall notify the Secretary of possession. CDC on July 12, 2002 published a notice that states that each facility should designate a responsible facility official (RFO) to complete the notification of possession form by September 10, 2002. The notice stated that to complete the notification form the RFO would need to inventory its facility and consult with others (e.g. principal investigators) as necessary to obtain information required for the notification form. Variola major was listed on that notification form. Neither NIH nor FDA identified the possession of Variola major.

The select agent regulations (42 CFR Part 73) became effective on February 7, 2003. These regulations require the registration of the possession, use, and transfer of select agents and toxins including Variola major and Variola minor virus. The registration application submitted by NIH as required under the select agent regulations did not include Variola major and Variola minor virus.

#### **Assessment of the Root Cause and Next Steps**

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) were ownership of the material is not clear or unknown.

DSAT is referring this incident to the HHS Office of Inspector General for further investigation and possible action.

**In order to address the findings noted above, please provide DSAT by August 22, 2014, the following:**

- 1. An updated security and incident response plan to address appropriate security and safety of select agents, or potential select agents, after identification in unregistered areas and during transfer between unregistered space and registered space.**
- 2. A copy of the completed "Phase 2" of NIH's plan, currently in development, aimed to address review and revision to NIH policies, potential changes to the NIH Table of Penalties, and establishment of enhanced management responsibilities at all levels of NIH. If the plan is not completed by August 22, 2014 please indicate when it will be completed and provide the completed plan by that date.**
- 3. Please clarify how the Biological Material Survey Attestation and the Phase I of the NIH Potential Hazardous Biological Materials Management Plan will address identification and the accountability for biological materials where ownership is not clear or unknown (e.g. the current incident where there was no Principal Investigator or other personnel specifically assigned to account for the collection containing Variola virus).**

**In addition, please provide the date by which NIH/DOHS will provide documentation that it has completed under Phase I of the NIH Potential Hazardous Biological Materials Management Plan the**

systematic compliance checks of all the laboratory spaces, all freezers and refrigerators, cold rooms, dry storage areas, etc. and has reviewed all inventories for potentially hazardous biological materials and the results of these checks with respect to select agents and toxins.

Please contact  
any questions regarding this report.

if you have

Sincerely,

**Captain, USPHS (Ret.)  
Department of Health and Human Services  
Centers for Disease Control and Prevention**

**Appendix E Supplement**

**House Energy and Commerce Committee**

**Supplemental Memorandum**



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

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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

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## 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.<sup>1</sup> 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

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<sup>1</sup> 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.<sup>2</sup> 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].”<sup>3</sup>

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.<sup>4</sup>

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.<sup>5</sup>

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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<sup>2</sup> 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).

<sup>3</sup> *Id.*

<sup>4</sup> 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).

<sup>5</sup> 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,<sup>6</sup> 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.<sup>7</sup>

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.<sup>8</sup> 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.<sup>9</sup> 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.”<sup>10</sup>

## 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.<sup>11</sup> In 2015, the Department of Defense (DoD) acknowledged that the Dugway Proving Ground, an

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<sup>6</sup> Interview with [FDA Researcher] conducted by H. Comm. on Energy & Commerce staff, April 6, 2014.

<sup>7</sup> 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).

<sup>8</sup> 42 U.S.C. § 262a.

<sup>9</sup> Justin Gillis, *NIH Denies It Has Smallpox Sample*, *WAS. POST*, Sept. 25, 1995.

<sup>10</sup> *Id.*

<sup>11</sup> 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<sup>12</sup> and DoD conducted internal reviews on each one of these events.<sup>13</sup> In contrast, neither the NIH nor the FDA have conducted an internal review on the discovery of the smallpox vials in 2014.<sup>14</sup>

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).<sup>15</sup> 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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<sup>12</sup> 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).

<sup>13</sup> 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 Ground*. 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.

<sup>14</sup> 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.

<sup>15</sup> 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.<sup>16</sup> 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.<sup>17</sup>

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.<sup>18</sup>

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.<sup>19</sup> NIH surrendered these vials of *B. anthracis* spores to the FBI Weapons of Mass Destruction Coordinator shortly after they were identified.<sup>20</sup> 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.<sup>21</sup> 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<sup>22</sup> 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).<sup>23</sup> 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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<sup>16</sup> Letter from Hon. Dr. Francis Collins, Director, NIH, to Hon. Fred Upton, Chairman, H. Comm. on Energy & Commerce (Sept. 17, 2014).

<sup>17</sup> *Id.*

<sup>18</sup> *Id.*

<sup>19</sup> NIH, Select Agent Investigative Report, Findings, Actions, Bethesda, MD, (June 5, 2012).

<sup>20</sup> *Id.*

<sup>21</sup> *Id.*

<sup>22</sup> Rocky Mountain Laboratories is an NIH facility located in Hamilton, Montana.

<sup>23</sup> 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.<sup>24</sup> 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.”<sup>25</sup> 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 11 of 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.”<sup>26</sup> DSAT ultimately placed NIH on a Performance Improvement Plan Program (PIPP).<sup>27</sup>

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.<sup>28</sup> 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.<sup>29</sup> 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

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<sup>24</sup> *Id.*

<sup>25</sup> Letter from Robbin Weyant, Director, CDC Division of Select Agents and Toxins, to Deborah Wilson, Responsible Official, NIH, (June 4, 2012).

<sup>26</sup> *Id.*

<sup>27</sup> *Id.*

<sup>28</sup> Letter from Thomas Kraus, Associate Commissioner for Legislation, FDA to the Hon. Fred Upton, Chairman, H. Comm. on Energy and Commerce (Sept. 18, 2014).

<sup>29</sup> *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.<sup>30</sup>

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,<sup>31</sup> and cited 42 CFR 73.17 several times.<sup>32</sup> 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.<sup>33</sup> Thus, even if the FDA was using NIH space, NIH's RO was responsible for the space.<sup>34</sup>

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

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<sup>30</sup> HHS-OIG, "Review of the National Institutes of Health Bethesda, Maryland, Laboratories' Compliance with Select Agent Regulations," A-03-09-00350, December 2009.

<sup>31</sup> *Id.*

<sup>32</sup> Email from Anne Tatem, NIH to Committee staff, April 13, 2016.

<sup>33</sup> Letter from Dr. Thomas Frieden, Director, CDC to the Hon. Fred Upton, Chairman, H. Comm. on Energy and Commerce (August 22, 2014).

<sup>34</sup> *Id.* at 6.

<sup>35</sup> 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.<sup>36</sup> 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.<sup>37</sup> 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.

<sup>36</sup> *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.

<sup>37</sup> 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.<sup>38</sup> 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.

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<sup>38</sup> *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.<sup>39</sup> 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.”<sup>40</sup> 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.”<sup>41</sup> The NIH RO further remarked that “it has nothing to do with cardboard boxes on shelves in which research materials may be stored.”<sup>42</sup> 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

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<sup>39</sup> *Id.*

<sup>40</sup> 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.

<sup>41</sup> Lena Sun, *House Panel Seeks Expanded GAO Review of Smallpox Incident at NIH*, WASH. POST (May 19, 2015).

<sup>42</sup> *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.”<sup>43</sup> 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.”<sup>44</sup> 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

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<sup>43</sup> NCI, Frederick Campus, Biosafety Technical Bulletin, November 2011.

<sup>44</sup> 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.<sup>45</sup> 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.<sup>46</sup>

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.”<sup>47</sup> 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.”<sup>48</sup>

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

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<sup>45</sup> Letter from Thomas Kraus, Associate Commissioner for Legislation, FDA to the Hon. Fred Upton, Chairman, H. Comm. on Energy and Commerce (Sept. 18, 2014).

<sup>46</sup> *Id.*

<sup>47</sup> Email from FDA counsel, to Committee staff (Dec. 11, 2014).

<sup>48</sup> *Id.*

number.”<sup>49</sup> 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.”<sup>50</sup> 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.

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<sup>49</sup> FDA, CBER Cold Room Policy (2011).

<sup>50</sup> 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.<sup>51</sup> 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.”<sup>52</sup> 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.”<sup>53</sup> 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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<sup>51</sup> 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).

<sup>52</sup> *Id.*

<sup>53</sup> 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.

**Appendix F Supplement**

**Potentially Hazardous Biological Materials**

**Management Plan**

**Phase 1**

## Potentially Hazardous Biological Materials Management Plan - Phase I

**Clean sweep of all NIH laboratories, clinical spaces, offices associated with laboratories – To Be Completed by September 30, 2014.**

**This clean sweep applies to all NIH owned or leased or contractor-operated laboratory spaces or facilities (e.g. off-site “freezer farms” and animal facilities) including RML, NIEHS, Frederick, Poolesville, etc.**

### **Phase I. Workplan**

**Step 1.** No later than July 11, the DDIR will inform the SDs of the need to execute a comprehensive search of all NIH laboratory spaces including all refrigerators, freezers (all types), cold rooms, cabinets, shelves, drawers, and storage rooms for potentially hazardous biological materials. There should be special emphasis on regulated materials such as Select Agents and Toxins, but other potentially hazardous biological materials such as infectious agents, non-regulated toxins, poisons, venoms, explosive materials, etc. should also be included.

**Step 2.** SDs will inform all PIs and other personnel in their ICs of the need to immediately commence a comprehensive search of laboratory and associated spaces including cabinets, drawers, shelves and all refrigerators, freezers (all types), cold rooms and storage rooms. SDs will instruct personnel to label materials properly that are maintained and appropriately discard all materials that are no longer needed, including unneeded materials left by former trainees and investigators. For identifiable clinical samples collected under IRB-approved protocols, special rules apply. Unidentified materials (unlabeled with uncertain contents) should be autoclaved twice. After double autoclaving, Medical Pathological Waste should be placed in a Medical Waste (MWP) (“Burn Box”) and dropped off at designated pickup locations. Any materials discharged to the drain must comply with NIH environmental standards for waste water discharge (see attached Waste Disposal Guide). No materials that are the subject of ongoing investigations or concerns should be destroyed. For materials thought possibly to include select agents, please contact the Division of Occupational Health and Safety (DOHS) in the Office of Research Services (ORS).

**Step 3.** SDs will assign responsible individual(s) to search common areas (such as cold rooms, instrument rooms, and freezers) and ensure that these areas are surveyed completely.

**Step 4.** Good laboratory practice indicates that a central list should be maintained by each PI of the nature of materials in each box, rack, or similar container in all storage areas in or around the laboratory or laboratory offices. This will require that the entire contents of each storage container be visually surveyed. All human pathogenic organisms that require BL2 level

containment and above, and biological toxins, venoms, or poisons (please see attached list of such compounds) must be recorded and inventoried as to location and reported to DOHS via an electronic registration system.

**Step 5.** PIs will be responsible for all spaces assigned to them and must survey all material and discard materials no longer needed.. Regulated but unregistered materials that may be found, such as Select Agents, must be turned over to Division of Occupational Health and Safety (DOHS) and All human pathogenic organisms that require BL2 level containment and above, and biological toxins, venoms, and poisons (please see attachment) must be recorded and inventoried as to location and reported to DOHS via an electronic registration system.

**Step 6.** PIs will sign an attestation that all potentially hazardous biological materials are properly labeled, stored, inventoried and any unlabeled materials were destroyed or turned over to DOHS. The attestations shall be collected and verified by the Scientific Director to make sure no areas were missed. (Attestation form is attached)

At this time, PIs should also ensure that all hazardous chemicals are properly labeled and stored or use this opportunity to contact the ORF Division of Environmental Protection for the proper disposal of unneeded or expired chemicals and chemical waste. This Division has been alerted to the need for possible expansion of service during this period and will assist promptly.

**Step 7.** PIs will sign, date and affix stickers to rooms and equipment indicating that under counter and upright freezers and refrigerators, cold rooms, laboratory doors and other closed spaces have been surveyed. **This includes freezers located in freezer farms (including those containing historical collections) or other leased or contracted space on and off campus.** (Stickers will be provided by DOHS)

**Step 8.** SDs will ensure and attest to OIR that all PIs in their IC have completed this clean sweep by **September 30, 2014.** (Attestation forms are attached).

**Step 9.** DOHS will perform systematic compliance checks of all the laboratory spaces, all freezers and refrigerators, cold rooms, dry storage areas, etc. including review of the inventories for potentially hazardous biological materials.

**Step 10.** For registered areas, DOHS will provide follow-up compliance checks of storage areas during annual surveys of registered laboratories (those conducting infectious disease and recombinant nucleic acid research). Safety specialists will document compliance checks in PI Dashboard.

**Reminder**

As a reminder, failure to comply with the requirements for select agents and toxins can lead to disciplinary actions including removal for an initial offense.

Select Agents and Toxins<sup>1</sup>: biological agents and toxins that could pose a severe threat to public health and safety, to animal health, or to animal products. See list attached. This plan is not limited to these Select Agents, but also includes all hazardous biological materials as defined above.

#### Select Agents and Toxins List

The following biological agents and toxins have been determined to have the potential to pose a severe threat to both human and animal health, to plant health, or to animal and plant products. An attenuated strain of a select agent or an inactive form of a select toxin may be excluded from the requirements of the Select Agent Regulations. The list of excluded agents and toxins can be found at: <http://www.selectagents.gov/Select%20Agents%20and%20Toxins%20Exclusions.html>.

**HHS AND USDA SELECT AGENTS AND TOXINS  
7 CFR Part 331, 9 CFR Part 121, and 42 CFR Part 73**

#### **HHS SELECT AGENTS AND TOXINS AND TOXINS**

Abrin  
Botulinum neurotoxins\*  
strain  
Botulinum neurotoxin producing species of *Clostridium*\*  
Conotoxins (Short, paralytic alpha conotoxins  
containing the following amino acid  
sequence X<sub>1</sub>CCX<sub>2</sub>PACGX<sub>3</sub>X<sub>4</sub>X<sub>5</sub>X<sub>6</sub>CX<sub>7</sub>)<sup>1</sup>  
*Coxiella burnetii*  
  
Crimean-Congo haemorrhagic fever virus  
Diacetoxyscirpenol  
Eastern Equine Encephalitis virus<sup>3</sup>

#### **OVERLAP SELECT AGENTS**

*Bacillus anthracis* \*  
*Bacillus anthracis* Pasteur  
  
*Brucella abortus*  
*Brucella melitensis*  
*Brucella suis*  
*Burkholderia mallei*\*  
*Burkholderia pseudomallei*  
  
Hendra virus  
Nipah virus  
Rift Valley fever virus

\*

Ebola virus\*  
encephalitis virus<sup>3</sup>  
*Francisella tularensis*\*  
Lassa fever virus  
Lujo virus

**AND TOXINS**

Marburg virus\*  
virus  
Monkeypox virus<sup>3</sup>  
Reconstructed replication competent forms of the 1918  
pandemic influenza virus containing any portion of the  
coding regions of all eight gene segments (Reconstructed  
virus\*

1918 Influenza virus)

Ricin

*Rickettsia prowazekii*

SARS-associated coronavirus (SARS-CoV)

Saxitoxin

South American Haemorrhagic Fever viruses:

virus

Chapare

Guanarito

Junin

virus

Machupo

Sabia

Staphylococcal enterotoxins A,B,C,D,E subtypes

**AND QUARANTINE (PPQ)**

T-2 toxin

**TOXINS**

Tetrodotxin

*pinensis (Peronosclerospora*

Tick-borne encephalitis complex (flavi) viruses:

Far Eastern

subtype

*a glycines)*

Siberian subtype

Kyasanur Forest disease virus

Omsk hemorrhagic fever virus

Variola major virus (Smallpox virus)\*

Variola minor virus (Alastrim)\*

*Yersinia pestis*\*

Venezuelan equine

**USDA SELECT AGENTS**

African horse sickness

African swine fever virus

Avian influenza virus<sup>3</sup>

Classical swine fever virus

Foot-and-mouth disease

Goat pox virus

Lumpy skin disease virus

*Mycoplasma capricolum*<sup>3</sup>

*Mycoplasma mycoides*<sup>3</sup>

Newcastle disease virus<sup>2,3</sup>

Peste des petits ruminants

Rinderpest virus\*

Sheep pox virus

Swine vesicular disease

**USDA PLANT PROTECTION**

**SELECT AGENTS AND**

*Peronosclerospora philip*

*sacchari)*

*Phoma glycinicola (formerly Pyrenochaet*

*Ralstonia solanacearum*

*Rathayibacter toxicus*

*Sclerophthora rayssiae*

*Synchytrium endobioticum*

*Xanthomonas oryzae*

\*Denotes Tier 1 Agent

1 C = Cysteine residues are all present as disulfides, with the 1st and 3rd Cysteine, and the 2nd and 4th Cysteine forming specific disulfide bridges; The consensus sequence includes known toxins  $\alpha$ -MI and  $\alpha$ -GI (shown above) as well as  $\alpha$ -GIA, Ac1.1a,  $\alpha$ -CnIA,  $\alpha$ -CnIB; X1 = any amino acid(s) or Des-X; X2 = Asparagine or Histidine; P = Proline; A = Alanine; G = Glycine; X3 = Arginine or Lysine; X4 = Asparagine, Histidine, Lysine, Arginine, Tyrosine, Phenylalanine or Tryptophan; X5 = Tyrosine, Phenylalanine, or Tryptophan; X6 = Serine, Threonine, Glutamate, Aspartate, Glutamine, or Asparagine; X7 = Any amino acid(s) or Des X and; "Des X" = "an amino acid does not have to be present at this position." For example if a peptide sequence were XCCHPA then the related peptide CCHPA would be designated as Des-X.

2 A virulent Newcastle disease virus (avian paramyxovirus serotype 2) has an intracerebral pathogenicity index in day-old chicks (*Gallus gallus*) of 0.7 or greater or has an amino acid sequence at the fusion (F) protein cleavage site that is consistent with virulent strains of Newcastle disease virus. A failure to detect a cleavage site that is consistent with virulent strains does not confirm the absence of a virulent virus.

3 Select agents that meet any of the following criteria are excluded from the requirements of this part: Any low pathogenic strains of avian influenza virus, South American genotype of eastern equine encephalitis virus, west African clade of Monkeypox viruses, any strain of Newcastle disease virus which does not meet the criteria for virulent Newcastle disease virus, all subspecies *Mycoplasma capricolum* except subspecies *capripneumoniae* (contagious caprine pleuropneumonia), all subspecies *Mycoplasma mycoides* except subspecies *mycoides* small colony (Mmm SC) (contagious bovine pleuropneumonia), and any subtypes of Venezuelan equine encephalitis virus except for Subtypes IAB or IC, provided that the individual or entity can verify that the agent is within the exclusion category. 9/10/13

**Appendix F Supplement**

**Potentially Hazardous Biological Materials**

**Management Plan**

**Phase 2**

## Potentially Hazardous Biological Materials Management Plan – Phase 2

*(retyped from the original)*

### Introduction

The NIH has embarked upon a comprehensive search of all research facilities to ensure that there are no select agents, toxins or hazardous biological materials improperly stored on our campuses. This effort is being referred to as “Clean Sweep” and is part of Phase 1 of the NIH Potentially Hazardous Biological Materials Management Plan. Phase 2 of this Plan addresses policy review and revision, potential changes to the NIH Table of Penalties and establishment of management responsibilities at all levels. Scientists often maintain materials for many years; sometimes for historical purposes but in many cases materials are abandoned or no longer needed or even useful. Phase 2 of the Work Plan is aimed at changing the research culture to one of accountability and responsibility in dealing with biological materials. The phase 2 Work Plan outlines the steps to be taken to ensure that responsibility and accountability for potentially hazardous biological materials becomes fully established as an expectation for NIH scientists and for the conduct of research at NIH. The Phase 2 Work Plan products and policies will apply to all NIH owned or leased or contractor-operated laboratory spaces or facilities (e.g. off-site “freezer farms” and animal facilities) including RML, NIEHS, Frederick, Poolesville, etc.)

### Phase 2. Work Plan

**Step 1.** Review and draft revisions for NIH Policy Manual Chapter 3035 – Working Safely with Hazardous Biological Materials will be completed. The revision will:

- expand responsibilities, at all levels, with regard to work with and management and storage of potentially hazardous biological materials at the NIH;
- institute and require upkeep of a central NIH inventory of potentially hazardous biological materials including Select Agents and Toxins, other potentially hazardous biological materials such as infectious agents handled at Biosafety Level 2 and above, non-regulated toxins, including poisons and venoms, and human blood, body fluids and tissues;
- require registration of potentially hazardous biological materials in storage (currently registration is only required when active work is being performed); and
- establish a requirement for disposition of materials when a scientist, post-doctoral fellow, student, etc. leave the NIH.

**Step 2.** NIH will review the NIH Table of Penalties to determine if failure to fully implement provisions of revised MC 3035 or failure to maintain adequate control of potentially hazardous biological materials warrants disciplinary action(s). Should it be determined that disciplinary actions are warranted, the Table of Penalties will be modified by the NIH Office of Human Resources.

**Step 3.** The Director, Division of Occupational Health and Safety, will work with the Deputy Director of Intramural Research to develop and implement, in all institutes performing biological research, a “check out” procedure for departing scientists that ensures all biological materials are transferred to another responsible party or destroyed prior to leaving NIH. Procedure will ensure that the NIH central database has been adequately updated to reflect the transfer of responsibility, destruction, or other disposition of the materials.

**Step 4.** In order to ensure that controls remain in place and are adequate:

- The NIH Division of Occupational Health and Safety will perform and document assurance checks of inventories maintained by registered laboratories (laboratories performing infectious disease and recombinant nucleic acid research, research using human or nonhuman blood and body fluids, or select agent laboratories) annually.
- Institute Health and Safety Committees will perform and document assurance checks of inventories maintained by non-registered laboratories annually.

**Appendix F Supplement**

**Annual Email Reminder: Select Agents and Toxins**

**From:** [ORS Information Line](#)  
**To:** [NIH-STAFF-DC-AREA@LIST.NIH.GOV](mailto:NIH-STAFF-DC-AREA@LIST.NIH.GOV)  
**Subject:** Annual Notification: Possession of Select Agents  
**Date:** Wednesday, March 25, 2015 9:33:42 AM

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This is the annual reminder that NIH employees cannot receive, possess, or ship Select Agents or Toxins unless authorized by the CDC Division of Select Agents and Toxins through the NIH Select Agent Program (Bethesda). Non-compliance can result in suspension of research, revocation of NIH's registration, or civil money penalties levied against you or against the NIH.

For your information, find links to:

- 1) a current list of Select Agents and Toxins - <http://www.selectagents.gov/SelectAgentsandToxinsList.html>.
- 2) a list of attenuated forms of some Select Agents that are not regulated (i.e., exclusions) - <http://www.selectagents.gov/SelectAgentsandToxinsExclusions.html>.
- 3) a list showing the aggregate amounts of the Select Agent toxins that are not regulated - <http://www.selectagents.gov/PermissibleToxinAmounts.html>.

Please note: the lists of exclusions and aggregate amounts are very specific. If you have any questions about what is considered a Select Agent or Toxin, or are interested in acquiring a Select Agent or Toxin, please contact the Select Agent Program. General information can be found at: <http://www.selectagents.gov>.

In addition, if you ever unexpectedly determine (via sequencing or some other analysis), that a sample in your possession contains a Select Agent or Toxin, and you are not authorized to possess that agent or toxin, you must notify the Select Agent Program immediately, even if the material has been inactivated. This refers to samples that you have no reason to suspect contain a Select Agent or Toxin. The NIH Select Agent Program (Bethesda) asks that you report this even if the sample is inactivated so that we can document disposition of the viable material that gave rise to the inactivated sample, and/or notify the sender of the material if it came from a collaborator.

If you have questions or concerns, please feel free to contact Antony Schwartz, Ph.D, Responsible Official, NIH Select Agent Program at 301-496-2960.

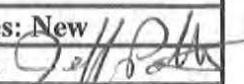
Thank you,

Antony Schwartz, Ph.D.  
Responsible Official – NIH Select Agent Program

Division of Occupational Health and Safety (DOHS)  
Office of Research Services  
National Institutes of Health  
13 South Drive, Bldg 13, Rm 3K04, MSC 5760  
Bethesda, Maryland 20892  
Phone: 301-435-7698, Fax: 301-480-0701  
E-mail: [antony.schwartz@nih.gov](mailto:antony.schwartz@nih.gov)

**Appendix F Supplement**

**SOP 902**

National Institutes of Health	Page 1 of 3
Biorisk Management Branch	SOP 902
Intra-Entity Transfer of Discovered Select Agents	Supersedes: New
	Approval: 
	Approval Date: 05-20-16

## I. Purpose

This standard operating procedure (SOP) describes the procedures for intra-entity transfer of select agents and toxins discovered in unregistered locations on NIH Campuses.

## II. Scope

The document applies to all NIH Campuses and all NIH Select Agent Programs (SAP).

## III. Roles and Responsibilities

NIH SAP personnel are responsible for following this SOP.

## IV. Special Practices

- ❖ Select agent(s)/toxin(s) must be transferred in a triple-packaging system designed to prevent leakage of materials.
- ❖ Packages must have a biohazard symbol on the outside.
- ❖ Select agent(s)/toxin(s) must be transferred with a chain-of-custody form (Appendix A) to ensure that they will not be left unattended.
- ❖ NIH SAP may seize select agent materials at any time. In such circumstances, the seizure of materials shall be documented using a chain-of-custody form.
- ❖ The RO/ARO will collect all the necessary information for filing a Form 3.

## V. Procedures

### A. **How to conduct an intra-entity transfer of select agents and toxins discovered in unregistered locations on NIH Campuses.**

1. If an ARO is first notified of the discovery of the select agent(s)/toxin(s) in an unregistered location, the ARO must notify the RO immediately.
2. The RO/ARO will instruct the individual(s) to secure the select agent(s)/toxin(s) and wait for the RO/ARO to arrive at the location.
3. Upon arrival, the RO/ARO will assess the circumstances surrounding the discovery of the select agent(s)/toxin(s) in the unregistered location and will collect all the necessary information for filing a Form 3.

4. If the assessment reveals that individual(s) were exposed to the select agent(s)/toxin(s), the RO/ARO will instruct the individual(s) to report to Occupational Medical Service immediately.
5. Following the procedures in the RO/ARO's incident response plan, the RO/ARO will notify CDC/DSAT or USDA/AgSAS File Manager about the discovery (phone, fax, email). The RO/ARO will document all non-email notifications with a follow-up email as soon as practically possible.
6. If a decision is made to remove the select agent(s)/toxin(s) from the premises, the RO/ARO will triple-package the select agent(s)/toxin(s) in a safe and secure manner and will complete a chain-of-custody form prior to transporting the select agent(s)/toxin(s).
7. The RO/ARO will transfer the select agent(s)/toxin(s) in a safe and secure manner to a registered select agent location. If a Form 2 is required, the RO/ARO will communicate with their File Manager to secure the necessary approvals.
8. Upon arrival, the RO/ARO will securely store the select agent(s)/toxin(s) or will make a decision to destroy them utilizing appropriate methods based on the agent(s)/toxin(s).
9. If a decision is made to destroy the select agent at the site of discovery, the RO/ARO will witness the destruction of the select agent(s)/toxin(s) and will document this destruction on the chain-of-custody form. An appropriate destruction method will be utilized based on the agent(s)/toxin(s) discovered.
10. When applicable, a biological indicator (BI) will be included with the destruction to validate the destruction method.

**B. Notifications**

1. The RO/ARO will make initial notifications to their File Manager following the procedures in the RO/ARO's incident response plan.
2. The RO/ARO will complete a Form 3 and submit it within 7 calendar days.
3. The RO/ARO will make the appropriate notifications up the chain-of-command as soon as possible.

**VI. References**

- 7 CFR 331
- 9 CFR 121
- 42 CFR 73
- Form 2 Instructions on FSAP website
- Form 3 Instructions on FSAP website

**VII. Appendices**

- A. Chain-of-Custody



NIH SELECT AGENT PROGRAM  
**Chain of Custody**



**Material Description:** \_\_\_\_\_

**From (print):** \_\_\_\_\_  
**ID#:** \_\_\_\_\_  
**Organization:** \_\_\_\_\_  
**Authorization Signature:** \_\_\_\_\_  
**Date (mm/dd/yyyy):** \_\_\_\_\_ **Time:** \_\_\_\_\_

**To (print):** \_\_\_\_\_  
**ID#:** \_\_\_\_\_  
**Organization:** \_\_\_\_\_  
**Authorization Signature:** \_\_\_\_\_  
**Date (mm/dd/yyyy):** \_\_\_\_\_ **Time:** \_\_\_\_\_

**From (print):** \_\_\_\_\_  
**ID#:** \_\_\_\_\_  
**Organization:** \_\_\_\_\_  
**Authorization Signature:** \_\_\_\_\_  
**Date (mm/dd/yyyy):** \_\_\_\_\_ **Time:** \_\_\_\_\_

**To (print):** \_\_\_\_\_  
**ID#:** \_\_\_\_\_  
**Organization:** \_\_\_\_\_  
**Authorization Signature:** \_\_\_\_\_  
**Date (mm/dd/yyyy):** \_\_\_\_\_ **Time:** \_\_\_\_\_

**Appendix F Supplement**

**PHBM Inventory Requirement**

PI NIH Username	PI Badgeid	PI/Responsible Person Information (Last Name, First Name)	Institute/Organization	City_State	Laboratory Name	Building	Room Number	Room Type	Equipment Detail	Storage Detail	Material Type	Material	Material Strain	# of Samples	Additional Description (optional)
schwartz	20064869	Schwartz, Antony	ORIS/DOHS	Bethesda, MD	Laboratory of Infectious Diseases	10	2N425	Cold Room	-80 Freezer, #123456	Top Shelf, Rack 1	Human Pathogen	Staphylococcus aureus	RN6290 wild type	25.00	Box 12

**Appendix F Supplement**

**Registration of Pathogens and rDNA Research**

<b>Draft Registration Document</b> Test registration for rDNA plus pathogen+Animal +HBBF	<b>rDNA/Pathogen</b>	<b>Accession Number</b> 16348-135440936	
<b>Principal Investigator</b> Baumann, Richard	<b>Organization</b> ORS-DOHS	<b>Email</b> baumannrg@mail.nih.gov	<b>Phone</b>
<b>Inactivated Registration</b>		<b>Date Submitted</b> N/A	<b>Expiration Date</b>

Doc Ver: 231-238

**Recommendations**

**Synopsis**

**Organism/Toxin:**

**Purpose:**

**Description:**

**Start Date of Project:**

**Duration of Project:**

**Points of Contact**

None

**Associated Laboratories**

Building/Room	Last Survey Date
13/3W84	10/17/2016

**Animal Laboratories**

Building/Room	Last Survey Date
13/test	06/23/2010

**Associated Researchers**

Name	Badge ID	Email	Work Type	e-Signed
Capul, Althea	2001192834	althea.capul@nih.gov	RD, HPRD, HBBF, Animal	No
Clarkson, Adam J.	0012011253	ac480y@nih.gov	RD, HPRD, HBBF, Animal	No

**Associated Registrations**

None

**Recombinant DNA**

**Sources of DNA:**

**Registration Document  
Approved by Biosafety Officer**

**Registration Document Approved  
by Chair, IBC**

**Registration Document  
Approved**

**Not Yet Approved**

Description of recombinant molecule(s) being used or created:

**Research Product**

Expression:

Expression Product:

Nature of Expression:

Product Exposed to:

Exposure Details:

Vector Use:

Proposed NIH Guidelines:

**Pathogen and/or Toxin**

Organism/Toxin:

Organism/Toxin Not in List:

Strain:

Volume > 10L:

Toxin Description:

Toxin Volume:

LD50 > 100 Nanograms:

Agent Inactivation:

Organism Concentration:

Containment:

Samples Repository:

Refrigerators/Freezers:

Cell Sorting/Tissue Grinding/Sonication:

Pathogenic or Toxic To:

Antibiotic Resistant:

Permit Required:

Select Agent:

Radiolabeled:

**Prokaryote Hosts**

Prokaryotic Host(s):

Description:

Uploaded Description:

Nature of Gene Sequence:

Percent Source Genome:

**Vector Plasmid DNA/Virus:**

**Uploaded Vector Maps:**

**Proposed NIH Guidelines:**

**Proposed Prokaryotic BSL:**

**Eukaryote Cells**

**Nature of Experiment:**

**Uploaded Documents:**

**Uploaded Vector Maps:**

**Expression of Foreign  
Gene:**

**Additional Uploaded Vector  
Maps:**

**Cloning of Toxin Molecule:**

**Proposed NIH Guidelines:**

**Proposed Eukaryotic BSL:**

**Animal Use 1**

**Animal Species:**

**Species is not in list:**

**Uploaded ASP(s):**

**ASP Number:**

**ASP Title:**

**Assertions:**

**Routes of Administration:**

**All Researchers Trained:**

**Containment BSL:**

**Practices BSL:**

**HBBF/Tissue Use**

**Register to Work With:**

**Types of Material:**

**Manipulation Techniques:**

**PI Attestations**

**Decontamination Plan  
Posted:**

**Staff Trained in Waste  
Disposal:**

**Research Staff Provided:**

**PI Certification:** Not certified

**Technical Competency:****Mitigation Programs:****PI E-Signature:** Registration is not complete**Dual Use Questionnaire**

A. Will the intermediate or final product of your experiments:

1. enhance the harmful consequences of the agent or toxin? (for example, will it enable weaponization\* of an agent or toxin, or enhance the virulence of a pathogen, or render a non-pathogen virulent?)
2. disrupt immunity or the effectiveness of an immunization against the agent or toxin without clinical or agricultural justification? (for example, make a vaccine less effective)
3. confer to the agent or toxin resistance to clinically or agriculturally useful prophylactic or therapeutic interventions against that agent or toxin or facilitate their ability to evade detection methodologies? (for example, confer a drug resistance trait to microorganism(s) in the study that could compromise the use of appropriate or conventional drugs to control or detect these microorganism(s) as disease agents in humans, veterinary medicine, or agriculture)?
4. increase the stability, transmissibility, or ability to disseminate the agent or toxin?
5. alter the host range or tropism of the agent or toxin?
6. enhance the susceptibility of a host population to the agent or toxin?
7. generate or reconstitute an eradicated or extinct agent or toxin?

B. Will synthetic biology\*\* techniques be used to construct a pathogen, toxin or potentially harmful product?

C. Even if your planned research does not involve any of the aforementioned criteria, and realizing your work or results could conceivably be misused, is there the potential for your data/product to be readily utilized to cause public harm?

Please add any important additional information you would like to share to address potential concerns.

After considering the above answers, do you believe there is the potential for your research data/product to be readily utilized to cause public harm?

\* In this context, weaponization refers to the enhanced dispersion, deliverability, survivability or pathogenesis of an agent or toxin.

\*\* Synthetic biology includes, but is not limited to, techniques of molecular biology, chemistry and genetics that would allow for the de novo synthesis or reverse engineering of genes, gene products or entire functional organisms.