Report to the Commissioner

FDA Review of the 2014 Discovery of Vials Labeled "*Variola*" and Other Vials Discovered in an FDA-Occupied Building on the NIH Campus

Director of Laboratory Science and Safety, FDA
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Summary

On July 1, 2014, during clean-up and inventory in preparation for a move of the Food and Drug Administration's (FDA) laboratories located at the National Institutes of Health's (NIH) campus in Bethesda, MD to FDA's White Oak campus in Silver Spring, MD, vials labeled as *Variola* (the virus that causes smallpox) were discovered. The six vials of *Variola* were found among another 321 unclaimed vials (for a total of 327 vials) inside cardboard boxes stored in the back left corner of an FDA laboratory's cold storage room.[1]

FDA's Director of Laboratory Science and Safety, Dr. Segaran Pillai, conducted this review with his team to further investigate the events surrounding the discovery of the vials labeled *Variola* and other biological agents. The report reflects interviews with FDA and NIH employees associated with the cold storage room in which the vials were discovered, a site-visit to the NIH campus, and a thorough review of all available reports and documentation relating to the discovery, including the "Joint CDC and FBI Investigation of Vials labeled '*Variola*' and other Vials Discovered on the NIH Bethesda, MD Campus." It includes a timeline of the events leading up to the discovery of the 327 vials on July 1, 2014; a detailed breakdown of the activities on the day the vials were discovered; and a description of the disposition of the 327 vials after discovery. The report concludes with a section describing corrective actions FDA has implemented to prevent this type of event from occurring in the future.

Upon discovery, the 327 vials were transferred to the NIH's Select Agent Program Responsible Official (RO). The RO secured the materials in a CDC registered select agent laboratory on the NIH campus in Bethesda, MD. The NIH RO then immediately notified the Federal Bureau of Investigation (FBI) and the CDC's Division of Select Agents and Toxins (DSAT) program of the discovery. The six vials labeled *Variola* (four vials labeled *Variola* and two vials labeled Alastrim, *Variola minor*), one vial labeled as RSSE (Russian spring-summer encephalitis virus), and nine other vials that could not be positively identified by their labels, were transferred to CDC on July 7, 2014, for evaluation. These vials were later destroyed at CDC, under the observation of WHO officials, on February 24, 2015. Of the remaining 311 vials, 32 vials were destroyed on the NIH campus on July 9, 2014. The remaining 279 vials were transferred to the National Biodefense Analysis & Countermeasures Center and either eventually destroyed (163 vials) or retained for research (116 vials) (see Table 1 for a description of the disposition of all 327 vials).

[1] The WHO declared the global eradication of smallpox in 1980 (WHO, Declaration of global eradication of smallpox (1980), http://apps.who.int/iris/handle/10665/155528). WHO recommended restricting the stock of *Variola* virus to the WHO collaborating center on smallpox and other poxvirus infections designated at the U.S. Centers for Disease Control and Prevention (CDC), and the Russian State Research Centre of Virology and Biotechnology. Subsequently, in 1996, WHO further recommended destruction of all remaining *Variola* virus by June 30, 1999 (WHO, Smallpox eradication – destruction of *Variola* virus stocks (1996), http://apps.who.int/iris/handle/10665/179420).

Timeline of Events

1946-1964	Over this approximate period of time, the 327 total vials that were discovered on July 1, 2014, were created. This is based on the information present on the vial labels. It is unknown what entity created the vials and when or how the vials came to be stored in Building 29A, Room 3C16 at NIH (see Table 1).
1968	Building 29A was constructed on the NIH campus, which, among other programs, housed NIH's Division of Biological Standards.
July 1, 1972	The NIH's Division of Biological Standards was transferred to FDA, where it became the FDA Bureau of Biologics. The Bureau continued to be located in Building 29A on the NIH campus.
1992	A Senior Investigator with the Center for Drug Evaluation and Research (CDER), FDA, began using the cold storage room (Room 3C16 in Building 29A) on NIH's campus. The cold storage room was a shared space between FDA laboratories from 1992 until 2014 when FDA moved its laboratories from the NIH campus to FDA's White Oak Campus. The Senior Investigator recalls that the cold storage room was not empty when he began using the cold storage room in 1992.
July 1, 2014	The collection of 327 sealed glass vials of pathogens and biological materials were discovered.

- ~11:30 a.m.-12:30 p.m.: The Senior Investigator was working in cold storage room 3C16 in Building 29A, preparing for the physical laboratory move from the NIH's campus to FDA's White Oak Campus.

- ~12:30 p.m.: The Senior Investigator investigated the contents of 12 brown cardboard boxes, which he did not own, located on a shelf in the back left corner of the cold storage room. The Senior Investigator discovered the glass vials with typed labels. One vial of lyophilized material had a typed label that stated "*Variola*."

- ~1:00 p.m.: The Senior Investigator informed the Director, Division of Viral Products, at FDA's Center for Biologics Evaluation and Research (CBER).

- ~1:00 p.m.-1:30 p.m.: The Senior Investigator and the Director, Division of Viral Products, looked through additional boxes.

- ~1:30 p.m.: The Senior Investigator and the Director, Division of Viral Products, finished their investigation of the boxes, left them in the cold storage room and went to the office of the Director, Division of Viral Products', supervisor, the Associate Director of Research. The Associate Director of Research was not in her office. The Director, Division of Viral Products, emailed her indicating that he would like to have a discussion upon her return.

- ~4:30 p.m.-5:00 p.m.: The Associate Director of Research emailed the Director, Division of Viral Products, indicating that she had returned to her office and was available to talk.

- ~5:00 p.m.: The Director, Division of Viral Products, went to the office of the Senior Investigator, the two then proceeded to the Associate Director of Research's office and informed her of the aforementioned events leading to the discovery of the vials labeled "*Variola*" and with the names of other pathogens discovered.

- ~5:30 p.m.: The Associate Director of Research contacted the NIH Select Agent Program Responsible Official (also the Director, Division of Occupational Health and Safety, NIH). The NIH Select Agent Program Responsible Official instructed the Associate Director of Research to transport the material to NIH's Division of Occupational Health and Safety (DOHS) office on the third floor of Building 13.

- ~5:35 p.m.: The Associate Director of Research contacted the Director, Division of Viral Products, and the two of them met in the cold storage room 3C16. They did not open any boxes and placed all 12 boxes into a larger cardboard box. The used lab coats and gloves were also placed into the larger box with the 12 smaller boxes. The larger box was sealed with clear packaging tape, and the Associate Director of Research alone hand-carried the material to the NIH's DOHS office on the 3rd floor of Building 13.

- ~5:50 p.m.: The Associate Director of Research arrived and met the NIH Select Agent Program Responsible Official at the NIH's DOHS office. The NIH Select Agent Program Responsible Official initiated a chain of custody form to document the transfer of the material from FDA to NIH's DOHS. The NIH Select Agent Program Responsible Official and the Associate Director of Research proceeded to the biosafety level 2 (BSL2) laboratory, Building 13, room 3W84 (a CDC registered select agent laboratory). The Associate Director of Research remained outside of 3W84, but watched through the window as the NIH Select Agent Program Responsible Official disarmed and entered the biosafety level 3 (BSL3) laboratory, 3W84B, and placed the material in the biosafety cabinet within 3W84B. The Associate Director of Research walked back to her office in the Building 29 complex and notified her supervisor, at that time, the Director of FDA's CBER.

  As of 6:00 p.m., July 1, 2014, FDA was no longer in possession of the 327 vials.

- 6:00 p.m.-6:08 p.m.: The NIH Select Agent Program Responsible Official tried three times to get in contact with the FBI. The FBI made contact with the NIH Select Agent Program Responsible Official at 6:28 p.m.

- 6:35 p.m.: The NIH Select Agent Program Responsible Official called and notified the director of the CDC's DSAT.

July 7-9, 2014	FBI and CDC's DSAT conducted a joint investigation. 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. It was noted that the integrity of one vial was compromised (labeled Nor. SPL. ANT – presumed to be Normal Spleen Antigen – which is neither a pathogen nor a Select Agent or Toxin).
July 7, 2014	Of the 327 vials, six vials that were believed to contain *Variola* (four vials labeled *Variola* and two vials labeled *Alastrim, Variola minor*), one vial labeled as RSSE (Russian spring-summer encephalitis virus), and nine other vials that could not be positively identified by their labels, were transferred to CDC custody for confirmation and destruction.
July 9, 2014	Of the remaining 311 vials, 32 were destroyed on the NIH's Bethesda Campus.
August 4, 2014	The remaining 279 vials were transferred to the National Biodefense Analysis & Countermeasures Center (NBACC).
August 4, 2014	Seven of the 279 vials were retained at NBACC for research purposes.
January 13, 2015	106 of the 279 vials were transferred to the United States Army Medical Research Institute of Infectious Diseases (USAMRIID) for research purposes.
January 15, 2015	Three of the 279 vials were transferred to the CDC for research purposes.
January 29, 2015	The remaining 163 of the 279 vials were destroyed at NBACC.
February 24, 2015	The 16 vials transferred to CDC on July 7, 2014, were destroyed by CDC under WHO observation.

Findings and Corrective Actions

As part of FDA's investigation, FDA employees associated with the cold storage room where the vials were discovered were interviewed, a site-visit to the NIH campus was conducted, and all available reports and documentation relating to the discovery were reviewed. This section describes the findings as a result of those interviews, and the corrective actions FDA has undertaken to prevent a similar occurrence from happening in the future.

Finding #1: The security and inventory control of orphaned biological materials (material whose owner departed the lab, but did not properly remove, destroy, or transfer the material to a new owner) was not maintained.

Corrective Action

Enact policies and procedures to ensure that biological material is not orphaned when its owner departs the laboratory.

Actions Taken to Date

- When a laboratory scientist departs the laboratory space, FDA's Staff Manual Guide (SMG) 2130.8[2], Section 3.D (effective January 13, 2016), requires that hazardous biological agents and toxins (HBATs) are either transferred to a new owner or destroyed.

- FDA has developed a Laboratory Scientist Onboarding and Exit Checklist that will be used throughout FDA to monitor and control HBATs.

Future Action

- FDA will conduct periodic, and unannounced, audits to ensure compliance with SMG 2130.8 and that all HBATs are controlled and managed by responsible individuals. These audits will include a review of the Checklists.

Finding #2: There was no single individual responsible for the entire contents and operation of the shared cold storage area.

Corrective Action

Enact policies and procedures to ensure that a single individual is responsible for all contents, including HBATs, in shared storage areas.

Action Taken to Date

- SMG 2130.8, Section 3.F, requires that one individual is responsible for each unit (shared or not) that stores HBATs. The unit must be clearly labeled to identify the individual who is responsible for its contents.

Future Action

- FDA will conduct periodic, and unannounced, audits to ensure compliance with SMG 2130.8 and that all storage areas are controlled and managed by responsible individuals.

[2] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/StaffManualGuides/UCM481698.pdf

Finding #3: FDA did not conduct a complete inventory of all of its laboratories and associated spaces when smallpox was eradicated in 1980 and all biological agents that cause smallpox were consolidated under the WHO Collaborating Centre repositories at the CDC (see footnote 1). FDA also did not conduct a complete inventory when the Federal Select Agent Program was enacted in 2003.

Corrective Action

Conduct a full inventory of all units that store HBATs, and require periodic updates to ensure the inventory list remains current at all times.

Actions Taken to Date

- In the months that followed the discovery of the vials, FDA conducted a thorough inventory of all storage areas, including areas that were not anticipated to contain HBATs. FDA now has a full account of all HBATs at all FDA-owned and operated facilities. This will also allow FDA to support future guidance and/or rules pertaining to biological agents and toxins if the CDC or APHIS decides to add a new agent or toxin to the Federal Select Agents and Toxins list.

- SMG 2130.8, Section 3.G, requires that a current, electronic inventory is maintained for all units that store HBATs.

Future Actions

- In fiscal year 2017, FDA will deploy a central electronic inventory system that will catalog all HBATs stored within the Agency.

- FDA will conduct periodic, and unannounced, audits to ensure compliance with SMG 2130.8 and that all HBATs are properly recorded in the inventory.

Finding #4: FDA did not follow the CDC Select Agent Guidelines for the packaging and transfer of samples to a high containment facility for securing the materials.

Corrective Action

Enact appropriate policies and procedures to ensure that individuals are aware of the proper actions to take when they encounter a select agent or toxin in an unregistered facility or laboratory for which they are not trained to handle.

Actions Taken to Date

- The procedure for the immediate remediation of inventory discrepancies, security breaches, or release of materials is provided in SMG 2130.8, Section 3.H.2.

- In addition to this guidance, FDA is currently developing clear communication tools, additional procedures, and standard forms to efficiently and responsibly respond to inventory discrepancies as appropriate to the level of risk. This is expected to be completed in the first half of fiscal year 2017.

Future Action

- FDA will continue to provide training for proper packaging, transfer, and transport of HBAT's and select agents and toxins to ensure safety and security.

Finding #5: The timeline of events show a delay between the discovery of the vials and the notification of appropriate officials.

Corrective Action

Enact procedures to ensure that individuals are aware of the proper officials to contact immediately when there is a safety or security incident.

Action Taken to Date

- The procedures for the immediate remediation of inventory discrepancies, security breaches, or release of materials are provided in SMG 2130.8, Section 3.H.2.
    - Officials (including the safety officer and the Director of Laboratory Science and Safety) must be immediately notified upon discovery of biological select agents and toxins in non-select agent registered laboratories or if the inventory cannot be physically located.
    - An immediate vial-by-vial audit must be performed to identify the scope of the discrepancy.

Future Action

- In fiscal year 2017, FDA will continue to emphasis the importance of timely notification and training to ensure that employees are aware of who to contact when there is a safety or security incident.

Finding #6: The storage area did not follow the best practices to prevent mold growth. There is evidence that cardboard was routinely stored in the cold storage room. Also, materials (e.g., boxes and other laboratory equipment) were stored on the floor.

Corrective Action

Communicate the best practices to ensure that individuals are aware of the proper way to store materials in a cold room.

Future Action

- In fiscal year 2017, DLSS will continue to implement the best practice of avoiding cardboard in locations where mold growth is likely and ensure that cold rooms are not used for storage of equipment that is not in use.

Compliance Mechanisms

- If an employee fails to comply with policies and procedures, the Agency may, as appropriate:

- temporarily transfer HBATs from the employee's possession or use for a period of time,
- permanently transfer HBATs from the employee's possession or use,
- enroll the employee into a Performance Improvement Plan, or
- take official action in coordination with the Office of Human Resources.

Table 1: Summary of Disposition of the 327 vials

Retained at NBACC for research purposes	7
Transferred to USAMRIID for research purposes	106
Transferred to CDC for research purposes	3
Transferred to CDC for destruction	16
Destroyed at NIH	32
Destroyed at NBACC	163
Total	327