



SEP 17 2014

National Institutes of Health
Bethesda, Maryland 20892
www.nih.gov

The Honorable Fred Upton
Chairman
Committee on Energy and Commerce
U.S. House of Representatives
Washington, D.C. 20515-6115

Dear Mr. Chairman:

Thank you for your July 28 letter to the National Institutes of Health (NIH) requesting information about a recent incident in which six vials of smallpox were found on the NIH campus in cold storage previously utilized by the Food and Drug Administration (FDA). Your letter also requested information regarding the NIH's management of the National Science Advisory Board for Biosecurity (NSABB).

Discovery of Smallpox Vials in an FDA Laboratory on the NIH Campus

With regard to the discovery of the vials of smallpox, it is important to note—as reflected in the enclosed answers to your questions—that the NIH maintains a rigorous program of biosafety oversight that includes laboratory inspections, biosafety training, and immediate corrective actions for any problems uncovered. The discovery of the vials of smallpox led to implementation of a corrective protocol that included immediate containment of the material and notification of proper authorities. Since then, a comprehensive search has been initiated by laboratory personnel of all freezers, refrigerators, cold rooms, and other storage areas to ensure that there are no select agents stored inappropriately. So far, we have found a small number of instances where select agents were improperly stored and these were included in an interim report. A final sweep is expected to be complete by September 30, 2014. The NIH is also verifying and updating its human pathogens inventory, across all institutes and facilities. Furthermore, all investigators must sign an attestation that storage areas have been fully inventoried.

Measures like these will continue on an ongoing basis, and the NIH will remain transparent in reporting on any developments pertinent to this incident. We welcome your questions and any suggestions your committee might offer. Conducting research safely and maintaining public trust is of paramount importance to the NIH.

Please find in Appendix A answers to your specific questions regarding the inspection and oversight of the FDA laboratories on the NIH campus.

Management of the National Science Advisory Board for Biosecurity (NSABB)

Your letter expresses concern about the recent rotation in the membership of the NSABB. The rotation of NSABB committee members is part of a routine process that all federal advisory

committees undergo to obtain fresh and diverse perspectives on the issues, per the rules implementing the Federal Advisory Committee Act (FACA). The replacement of members is typically staggered to safeguard against the loss of institutional memory and knowledge. Thus, only a portion of the committee is replaced at any one time. Under special circumstances, membership terms can be extended, though not indefinitely. The decision regarding the replacement of members is predicated on a number of considerations including, but not limited to, a member's length of service and the availability of their replacement. When the new member is available, a member serving an extended term is typically notified of the conclusion of his or her service.

Those individuals who recently received notification that their service on the NSABB had come to an end were the last among the original board members and were serving under an extension of their original terms. These individuals were to serve under extended terms until replacement members were identified or until 2015 and, as noted above, their replacement was part of the routine process of turning over committee membership. The NIH and other federal agencies are grateful for the departing members' dedication and contributions to NSABB activities during their terms of service. Given their experience on the board, and in their professional lives, these members' views will continue to be valued, and they are invited and encouraged to attend the next meeting of the NSABB in their individual capacities.

Your letter also notes that the NSABB has not met in almost two years. The NSABB is convened when the government requires advice on matters regarding biosecurity oversight of dual use research of concern (DURC). Up until its most recent meeting, the NSABB spent much of its effort advising on the development of policies related to the conduct, communication, and oversight of dual use research. The NSABB accomplished much in that regard, and the government has been taking the Board's recommendations into consideration in the process of developing policy on the federal and institutional oversight of dual use research of concern. In the interim since the NSABB's last meeting, it has not been necessary to convene the Board, but we anticipate reconvening the NSABB in the fall of 2014.

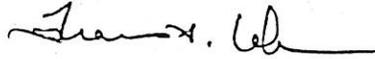
In addition, your letter references the changes in the taskings to the NSABB, as reflected in the revisions to its charter over time. In general, the government assesses what advice it needs from FACA committees, such as the NSABB, and then considers whether to modify the charter accordingly when it is next up for renewal. For example, the NSABB was established primarily to be a source of advice on the development of DURC policies and, as noted above, has fulfilled its charge in that regard, and so its charge was modified accordingly. That notwithstanding, the charter includes a provision for the NSABB to take up other issues as directed by the HHS Secretary, and this provision offers latitude with respect to matters on which the NSABB may be asked to advise.

Finally, your letter requested the NIH provide all e-mails since January 1, 2012, in the possession of Dr. Mary Groesch relating to the NSABB, including the dismissal of the eleven members of the Board, the change in the Board's charter, and why the Board has not met in nearly two years. These are being compiled and will be provided shortly under separate cover.

Thank you for allowing us to provide this information. We hope it is useful to the Committee. If you have any further questions about the issues discussed or require any follow-up information, please contact me.

I am sending a similar response to the co-signatories of your letter.

Sincerely yours,



Francis S. Collins, M.D., Ph.D.
Director

Enclosures

cc:

The Honorable Henry A. Waxman, Ranking Member
The Honorable Diana DeGette, Ranking Member,
Subcommittee on Oversight and Investigations

APPENDIX A

NIH Response to Questions Posed by the Committee on Energy and Commerce (July 28, 2014)

As a helpful context for the answers provided below to your questions, the NIH would like to first clarify the management and oversight relationship between the NIH and the FDA with respect to the Building 29 complex.

The Food and Drug Administration (FDA) is a tenant on the NIH campus. The FDA is the sole occupant of three buildings, Buildings 29, 29A, and 29B, normally referred to as the Building 29 Complex.

With respect to the Building 29 complex, the NIH is responsible for providing support services to the FDA that include building maintenance, waste and environmental services, occupational medical and safety and health services. Biosafety support is also a component of the safety and health services provided to FDA laboratories. The NIH also provides the services of the NIH Institutional Biosafety Committee (IBC) to the Building 29 complex laboratories. Laboratories conducting research with infectious disease agents, recombinant or synthetic nucleic acid molecules, and human or nonhuman blood, body fluids, and tissues are required to register with the NIH IBC. The FDA laboratories in 29A that conducted research involving these materials were registered with the IBC. Registration of these laboratories with the NIH IBC leads to annual NIH safety surveys (inspections) of the areas identified as conducting these types of research by the Principal Investigator. The NIH only conducts safety surveys of laboratories registered by Principal Investigators. The cold room in question, where the smallpox vials were found, was not registered with the NIH.

The NIH only provides biosafety and other support services to the FDA. FDA management and other agencies with requisite authority have oversight responsibility.

- 1. The smallpox samples and the other discovered vials of pathogens are dated well before 1972. The lab facility where these vials were discovered was reportedly transferred from the NIH to the FDA in 1972. Did the NIH transfer the ownership of the biological samples to the FDA? If yes, provide copies of documents related to the transfer of ownership of biological materials or samples in the labs. If not, were these vials still legally the property of the NIH? Provide the legal basis for the conclusion.**

The NIH has no records of this transfer. The collection may not have been property of, originated at, or been transferred from the NIH. At this time, the FBI is performing a due diligence investigation to attempt to determine the origin of the collection and legal ownership of the samples. The only information provided to the NIH, regarding these boxes, was provided by an FDA employee who stated that the boxes had been sitting in the cold room for at least twenty years since his arrival at FDA.

- 2. Has the NIH ever had a Memorandum of Understanding (MOU) with, or including the FDA relating to the FDA laboratories on the NIH campus? If so, provide copies of any MOUs since the 1972 transfer or around the time of the 1972 transfer.**

We understand the question to refer to any agreements that the NIH and the FDA entered into relating to the FDA laboratories on the NIH campus. The NIH and the FDA entered into a series of Interagency Agreements under which the FDA reimbursed the NIH for services that the NIH

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provided the FDA for the laboratories in Building 29. We have attached copies of these Interagency Agreements for the period from 2002 to present, the timeframe for which this documentation is available. Please see Attachment 1, which is being provided under separate cover.

3. **Does the NIH have a responsibility to conduct inspections of the FDA laboratories on the NIH campus to ensure the laboratory is meeting the specific level of biosafety designated to that facility and research to ensure safe handling of biological agents?**

Yes, as explained in the introduction, the NIH conducts safety inspections of all laboratories, including the FDA laboratories in Building 29A, registered to work with human pathogens at Biosafety Level 2 (BSL-2) or higher laboratories conducting non-exempt recombinant nucleic acid research, as defined in the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*, and those laboratories working with human and nonhuman primate blood and body fluids. These inspections are scheduled and performed at least annually for registered laboratories.

4. **Have the FDA laboratories in Building 29A ever been inspected by the NIH? If so, please provide copies of any inspections conducted since 2002?**

Yes. Please see answer to question three above. Copies of NIH inspections of Building 29A are included in Attachment 2, which is being provided under separate cover.

5. **Have the FDA laboratories in Building 29A ever been inspected by the CDC and/or the Department of Agriculture's Animal and Plant Health Inspection Services (APHIS)? If so, please provide copies of any inspections conducted since 2002.**

Yes, copies of CDC and APHIS inspection reports that reference Building 29A are included in Attachment 3, which is being provided under separate cover.

6. **Have the FDA laboratories in Building 29A ever been inspected or audited by another federal agency or any other kind of external review group? If so, please provide copies of any inspections or audits conducted since 2002.**

For details on inspections or audits conducted by any other federal agencies or external review group please contact FDA management responsible for the laboratories.

7. **Provide a list of all NIH and FDA laboratories in Building 29A prior to June 1, 2014 with the associated area of research.**

There are no NIH laboratories or personnel located in the Building 29 Complex. The FDA can provide a list of its laboratories in Building 29A, and we understand that the FDA will be doing so in response to a request you have sent them.

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8. Does the NIH have a responsibility to account for all select agents being stored in any facility on the NIH campus?

Yes, the Select Agent Responsible Official is responsible for the Select Agents that have been registered on campus, as described above. Per the *NIH Policy Manual Chapter 3035 - Working Safely with Hazardous Biological Materials*, it is the Principal Investigator's responsibility to declare these materials to the Select Agent Responsible Official to initiate the select agent registration process.

9. Has the NIH conducted any inventory checks of select agents of any lab in Building 29A, including the FDA labs?

Yes. Quarterly inventory checks were conducted in all registered select agent laboratories of the registered select agents. By law (7 CFR Part 331, 9 CFR Part 121, 42 CFR Part 73), inventories must be kept of select agent materials held in long-term storage. The select agent regulations require an accurate and current inventory for: (1) "each select agent (including viral genetic elements, recombinant and/or synthetic nucleic acids, and recombinant and/or synthetic organisms) held in long-term storage (placement in a system designed to ensure viability for future use, such as in a freezer or lyophilized materials)." The cold room where the vials containing smallpox were discovered was not identified by the FDA as containing select agents and therefore no select agent inventory was conducted in this cold room.

10. Was it ever the practice of NIH scientists to maintain collections of pathogens? If yes, when? Has the NIH ever found collections of pathogens in storage at NIH laboratories?

Yes, at the NIH 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 laboratories is common practice.

11. Provide a list of NIH officials responsible for overseeing the FDA labs on the NIH campus.

The NIH only provides biosafety and other support services to the FDA. FDA management and other agencies with requisite authority have oversight responsibility.

12. Did the NIH ever conduct an inventory check accounting for all select agents on the NIH campus after 9/11 and the anthrax mailings? If not, why not? If so, were the FDA labs in Building 29A included? If the FDA labs were not included, why not?

The NIH routinely checks select agent inventories in compliance with 7 CFR Part 331, 9 CFR Part 121, and 42 CFR Part 73. FDA select agent laboratories on the NIH campus are included in these checks. However, the space in which the smallpox was found was not registered with the NIH for storage or work with Select Agents.

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13. Please identify all instances of discovery of select agents in unregistered locations at NIH since 2002. Include the dates, the locations, identity of the select agents, and action taken.

In February 2012, during an inspection of a registered laboratory, the NIH discovered vials of *Bacillus anthracis* spores housed in an unregistered space in Building 33 on the NIH Bethesda campus. 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.

Based on this finding, the NIH embarked upon 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. During this inspection, the NIH found other instances of regulated, but **non-infectious** anthrax, in three other locations: Building 14A, Room 162; Bldg 29 A, Room 3A19; and Bldg. 6A, Room 2A02. Upon discovery of inappropriate storage of the regulated *B. anthracis* strains, the NIH immediately notified the CDC Division of Select Agent and Toxins and then rapidly and proactively embarked upon an extensive investigation to ensure that no other regulated *B. anthracis* strains were inappropriately stored at the NIH. The findings of this investigation resulted in immediate changes to NIH Select Agent Program procedures; administrative actions including proposals of disciplinary action; and management actions resulting in NIH-wide activities to further ensure appropriate use and storage of select agents at the NIH.

Administrative Actions Taken

- 1) The NIH Select Agent Program (SAP) identified the need to expand documentation beyond that required by the Select Agent regulations. Procedures were changed to provide notification and documentation to every Select Agent Principal Investigator/Supervisor when an individual has been removed from the program or access to select agent laboratories has been removed. This was instituted on February 7, 2012.
- 2) NIH SAP procedures have been modified to ensure that prior to de-registering a select agent space, storage areas do not contain "remnant" select agent materials. This was instituted February 7, 2012.
- 3) NIH SAP identified the need for PIs to agree, in writing, to their responsibility for the select agents in their possession from "cradle to grave." This was instituted February 7, 2012.
- 4) NIH SAP requested a complete accounting of everyone who has been issued a "hard" key to a select agent controlled space, from the NIH Locksmith, to ensure that only authorized personnel have access to these areas.

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- 5) Select Agent training materials were modified to further emphasize accountability, responsibility and the penalties associated with failure to adhere to select agent requirements.
 - 6) The Scientific Director of one Institute, in which select agents were inappropriately housed, suspended a non-compliant laboratory's privilege to conduct work with any human pathogen in addition to select agents.
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Management Actions Taken

The NIH Deputy Director for Intramural Research required that each NIH Intramural Principal Investigator, Senior Investigator, or Clinical Investigator attest, in writing, to the fact that they had surveyed their laboratory spaces for select agent materials and that none were found. If unregistered materials were found, the Investigator was required to contact the appropriate Responsible Official for the NIH location. Approximately 1,200 Principal Investigators from NIH Institutes that conduct intramural laboratory research, on any NIH campus, completed these written attestations. FDA personnel also completed the written attestations. The Scientific Director of each Institute was responsible for ensuring that all PIs complied with this requirement. This also included the FDA management. The completed attestation documents were reviewed and appropriate follow-up was provided by NIH Select Agent Program staff members. No select agents were identified during the survey and attestation process in 2012.

The Scientific Director, National Institute of Allergy and Infectious Diseases, where most select agent work is conducted, added a "Select Agent Compliance" element in Performance Management Appraisal Program Plans of all Principal Investigators working with select agents.

The NIH Deputy Director for Management initiated review of the NIH Table of Penalties with regard to its applicability to violations of the Select Agent regulations or NIH policies governing use of these agents. This review resulted in revision of the Table of Penalties to specifically address select agents. The revision referencing select agents was implemented on May 7, 2012, and is included below. **Please note:** NIH disciplinary actions with regard to select agent violations do not apply to FDA personnel working on the NIH campus.

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Select Agents and Toxins

NATURE OF MISCONDUCT	FIRST ACTION	SECOND ACTION	THIRD ACTION
A SINGLE ACT OF GROSS NEGLIGENCE CAN WARRANT REMOVAL FOR A FIRST OFFENSE.			
- PROCEDURAL OR ADMINISTRATIVE DEVIATION FROM PROCEDURES FOR THE POSSESSION, USE, OR TRANSFER OF SELECT AGENTS OR TOXINS OR OTHER REGULATED MATERIALS	REPRIMAND TO REMOVAL	14-DAY SUSPENSION TO REMOVAL	REMOVAL
- FAILURE TO PROPERLY SAFEGUARD OR SECURE SELECT AGENTS OR TOXINS OR OTHER REGULATED MATERIALS	REPRIMAND TO REMOVAL	14-DAY SUSPENSION TO REMOVAL	REMOVAL
- FAILURE TO PROPERLY DISPOSE OF SELECT AGENTS OR TOXINS OR OTHER REGULATED MATERIALS	REPRIMAND TO REMOVAL	14-DAY SUSPENSION TO REMOVAL	REMOVAL
Note: * Biological agents and toxins that could pose a severe threat to public health and safety, to animal health, or to animal products.			

* As defined by 42 Code of Federal Regulations (CFR), Part 73; 9 CFR, Part 121; and 7 CFR, Part 331.

In addition to the above incident, in September 2012, the NIH received a letter from APHIS stating that during one of its inspections they discovered a strain of Highly Pathogenic Avian Influenza in a room not registered for Select Agent research. It was the NIH's view that the strain was not in fact covered under the Select Agent regulations. The APHIS letter to the NIH, as well as our response can be found in Attachment 3, which is being provided under separate cover.