Taking another look—US Biosafety recommendations

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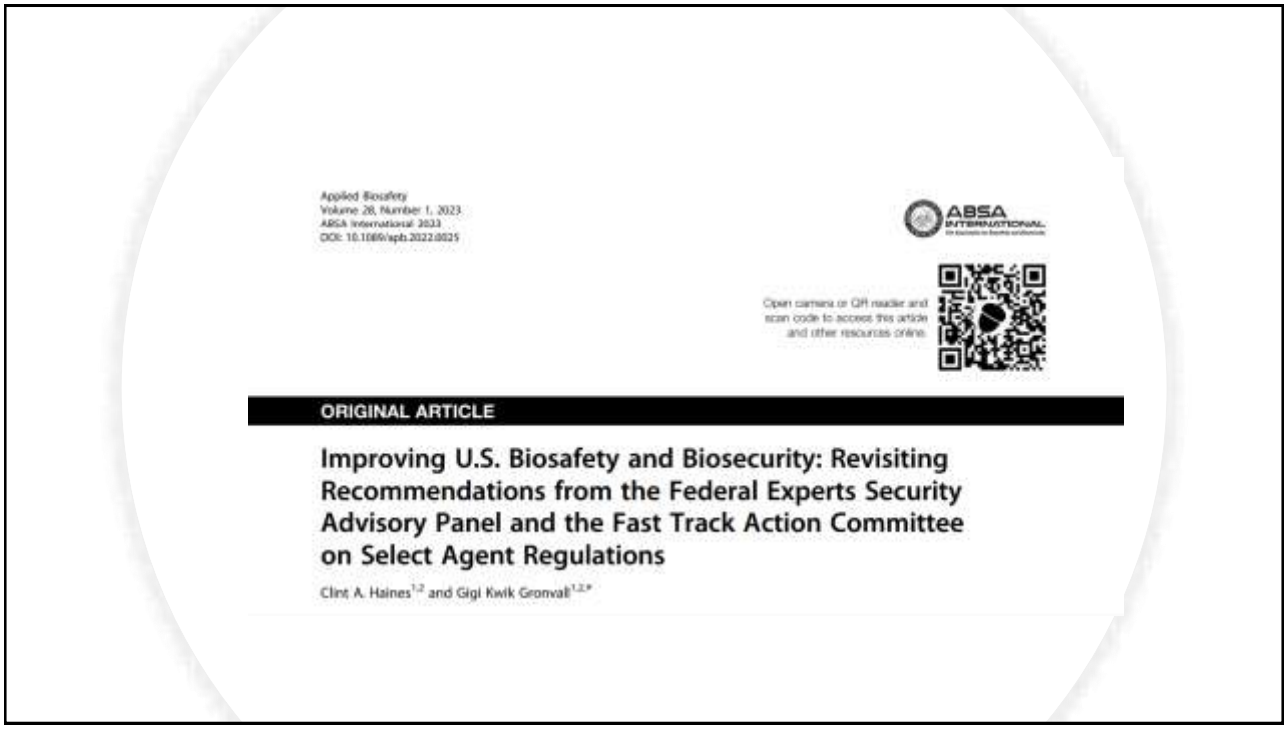


The Three Major Incidents of 2014

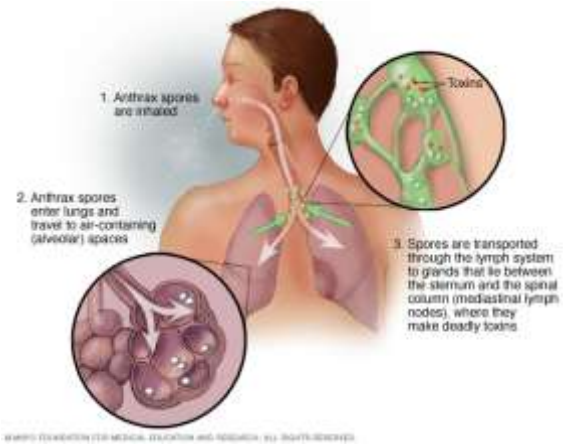
1: Cross contamination of LPAI with HPAI
- USDA Southeast Poultry Research Lab (Left)

2: Unvalidated inactivation procedure leads to potential anthrax exposures
- CDC Roybal campus (right)

3: Discovery of live unregistered smallpox samples in lab storage
- NIH Bethesda campus

January 17, 2014: CDC's Influenza Division

- Low pathogenic avian influenza (LPAI) was contaminated with high pathogenic avian influenza (HPAI)
  - Likely occurred due to a staff scientist not following procedural norms
  - Lack of team-specific standard operating procedure
- SEPRL requested sample of LPAI, and sample sent March 12, 2014
- SEPRL notified CDC ID about contamination May 23, 2014
- Contamination was confirmed, but chain of command not notified until July 14, 2014
- No exposures due to handling of LPAI at BSL3 level of containment



June 6-13, 2014: CDC Roybal Campus

- *B. anthracis* samples were inactivated using an invalidated procedure
  - Goal: Bring samples to BSL2 level of containment for experimentation
  - Impact: 75 CDC staff exposed to potentially viable bacteria
- Workers handled the samples using BSL2 PPE which was not appropriate for live *B. anthracis*
- Exposure discovered on July 13, 2014 when disposing of inactivation test plates
- Response:
  - All staff treated with antibiotics pre-emptively, and no disease reported
  - Labs and hallways tested for spores, and none found

Credit: Mayo Clinic. Source at end of presentation.

July 1, 2014: NIH Bethesda Campus

- Six sealed glass vials of freeze-dried smallpox found in NIH lab
  - Vials were in long-forgotten cardboard box from 1954
  - Samples transferred to CDC BSL4 lab for testing
  - At least 2 vials contained viable virus
- Result:
  - No vials breached out of containment
  - No workers exposed
  - Generated public scrutiny

Holdren-Monaco Memo: Intro

THE WHITE HOUSE

WASHINGTON

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conducted safely and securely. The United States Government has acted swiftly to address three recent U.S. biosafety and biosecurity incidents. To improve U.S. preparedness for such threats and incidents, it is imperative that infectious disease researchers: (1) conduct a comprehensive review of current biosafety and biosecurity protocols and procedures to ensure they are adequate and appropriate for today's infectious disease research; (2) inventory and document their culture collections; and (3) increase attentiveness throughout the research community

Holdren-Monaco Memo: Long-Term Steps

- Federal: United States departments and agencies have agreed to conduct a coordinated Federal review through an existing interagency committee to identify needs and gaps and make recommendations to optimize biosafety, biosecurity, oversight, and inventory management and control for BSAT and identify actions and any regulatory changes necessary to improve biosafety and biosecurity. The committee will build on

Holdren-Monaco Memo: Long-Term Steps

- Broad Stakeholder Engagement: In response to the three recent U.S. biosafety and biosecurity incidents, the National Science and Technology Council (NSTC) will establish an interagency group to conduct a comprehensive review of the impact that the Select Agent Regulations (SAR) have had on science, technology, and national security. The group should include in its review an analysis of benefits, costs, and limitations of the SAR, as well as offer recommendations to address any identified challenges or gaps. To support this process, the NSTC will convene a public meeting of SAR stakeholders to inform and support the NSTC-led process. The NSTC body will be identified or created within 30 days of the date of this memorandum and will provide recommendations directly to the Assistant to the President for Science and Technology within 180 days of identification.

Lisa O. Monaco
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Assistant to the President for Science and Technology

Our Study

- Analyzes progress in implementing recommendations from committees
  - Federal Experts Security Advisory Panel (FESAP)
  - Fast Track Action Committee on Select Agent Regulations (FTAC)
- Methods
  - Using open-source material
    - CDC & FSAP websites
    - Select Agent Regulations
    - News Sources
    - Notices of Proposed Rulemaking
    - Select Agent Grams
- Did actions address recommendations? Next Steps?

Recommendations by FESAP and FTAC Committees

Table 1. Completion status of recommendations from the Federal Experts Security Advisory Panel and the Fast Track Action Committee on the Select Agent Regulations

Category	Committee and number	Recommendation description	Result	Current status
Culture of responsibility	FESAP 1.1	Develop a research culture that emphasizes the responsibility each individual and institution holds in conducting biomedical research in a safe and ethical manner.	No specific language mentioning bioethics training to develop a responsible research culture was found in the SAR or FSAP Guidance for SAR Training Requirements.	
Oversight	FESAP 1.2	Ensure that structures capable of maintaining biosafety and biosecurity compliance are present at all institutions that perform research on infectious agents and toxins.	A biosafety and biosecurity compliance structure is addressed in the 6th edition of *BMBL* in the "Risk Communication" portion of "Section II—Biological Risk Assessment."	
Oversight	FESAP 1.3	Require research institutions to validate all laboratory policies and plans related to decontamination, inactivation, and sterilization of potentially infectious agents with a qualified review entity.	The SAR and the FSAP's Guidance on the Inactivation or Removal of Select Agents and Toxins for Future Use provide details on inactivation procedure validation and verification.	
Oversight	FTAC 11	The FSAP should establish a panel of subject matter experts who can provide timely advice on best practices and proposed changes to the SAR.	The FSAP took many steps to increase communication between the program and regulated entities, such as publishing NPRM for review and feedback, but a committee of experts was not created.	

Outreach and education	FESAP 1.4	Develop security awareness modules for regulated entities with an emphasis on incident reporting, infectious agent security breaches, and personal responsibility.	Language addressing security awareness training appears in 42 CFR 73 section 73.15(a).	
Outreach and education	FESAP 1.5	Develop biosafety and biosecurity communication strategies for increasing awareness.	The IBMWG was tasked with developing a communications plan and supporting outreach, but no information regarding a strategic communications plan was discovered.	
Outreach and education	FTAC 2	Develop a mechanism for the transparent release of information on BSAT research to the public.	A report on the FSAP is released annually to provide the public with information on BSAT research and laboratory incidents. However, more could be done to increase transparency and accessibility of the information for the general public.	
Outreach and education	FTAC 3	Develop a method for regulated entities to share biosafety and biosecurity best practices.	The FSAP hosted a 3-day seminar for responsible officials and established an independent forum for best practice exchange through the American Biological Safety Association.	
Outreach and education	FTAC 12	Increase collaborative discussions about BSAT research safety standards on an international stage.	The IEGBBR currently has 11 member nations that maintain a commitment to strong biosafety and biosecurity standards, but there are many nations that perform high-containment research that are not members of this group.	

Applied biosafety research	FESAP 1.6	Create a sustainable Federally funded program to perform research on applied biosafety best practices.	No information on a sustainable a sustainable applied biosafety research program to develop best practices and technologies for containment was discovered.	
Incident reporting	FESAP 1.7	Develop an anonymous, voluntary, and nonpunitive reporting system that could be used as a tool for learning and hazard training.	Leadership of this initiative was given to HHS and IBMWG, but no information could be found on an anonymous, voluntary, and nonpunitive BSAT incident reporting system that could be used as a tool for future training.	
Material accountability	FESAP 1.8	Increase awareness around best practice protocols for material accountability at registered entities.	Language addressing best practice protocols for material accountability and working stock inventory requirements can be found in 42 CFR 73 sections 73.17(a)(1) and 73.17(c), but more could be done to improve awareness of the regulations.	
Material accountability	FESAP 2.5	Provide increased guidance for how laboratories should handle inventory control and working stocks.	Language addressing best practice protocols for material accountability and working stock inventory requirements can be found in 42 CFR 73 sections 73.17(a)(1) and 73.17(c), but more could be done to improve awareness of the regulations.	
Material accountability	FTAC 6	Ensure that laboratories can maintain inventories of biological select agents without the need to characterize them quantitatively.	There is no language in the SAR requiring biological select agents to be characterized quantitatively, but more could be done to improve awareness of the regulations.	

Inspection process	FTAC 7	Develop a method to increase consistency between registered entity site inspections and across inspectors.	Site inspector training was performed in November 2017 to increase consistency, but a report from the OIG from June 2018 stated that inspectors still had insufficient training.
Inspection process	FTAC 8	Enhance communication between the FSAP and registered entities during site inspection process.	A process has been developed to provide registered entities with a preliminary report if the final report will not be available within 30 days of the site inspection. Data on report timeliness will be provided by the CDC annually.
Inspection process	FTAC 9	Develop a means to categorize inspection findings, so minor clerical errors are not considered as severe as major security breaches.	A document that categorizes violations based on severity was finalized in September 2017 with a goal of increasing site inspection consistency and enhancing transparency in how regulated entities are scored.
Inspection process	FTAC 10	Develop a process for registered entities to dispute issues found during site inspections.	A formal dispute mechanism was developed and released for use by regulated entities in March 2016.
Regulations and guidelines	FESAP 2.1	Require the documentation of BSAT drills and exercises.	Language requiring the documentation of BSAT drills and exercises was added to 42 CFR 73 sections 73.11(h), 73.12(e), and 73.14(f).

(continued)

Regulations and guidelines	FESAP 2.2	Require that BSAT trainees are instructed on how to access the OIG hotline to report safety concerns anonymously.	Language requiring that BSAT trainees are instructed how to access the OIG hotline was added to 42 CFR 73 section 73.9(a)(7).
Regulations and guidelines	FESAP 2.3	Require that responsible officials be included in a registered entity's biosafety and biosecurity committee.	Language requiring that Responsible Officials be included in a registered entity's biosafety and biosecurity committee was added to 42 CFR 73 section 73.11(f)(2).
Regulations and guidelines	FESAP 2.4	Require that biosafety and biosecurity oversight committees involve all stakeholders in the development of relevant programs.	Language recommending that biosafety and biosecurity oversight committees involve all stakeholders in the development of relevant programs is included in the introduction of "Section II—Biological Risk" in the *BMBL*, but no language is included in the SAR.
Regulations and guidelines	FESAP 2.6	Enhance biosafety plan development guidance.	Language enhancing biosafety plan development guidance was added to 42 CFR 73 section 73.12(a).
Regulations and guidelines	FESAP 2.7	Support the adoption of policies by registered entities that set a cap on maximum hours spent in high-containment.	There is currently no language in the SAR suggesting a cap on the maximum hours an individual can spend in high-containment. However, a Select Agent Gram from April 2016 states that the FSAP will not issue guidance on the topic but specifies that they support the recommendation.

Regulations and guidelines	FESAP 2.8	Support the development and release of the OSHA infectious disease standard.	The Biden Administration has announced plans to release a notice of proposed rulemaking for the OSHA infectious disease standard around October 2022 for public review and comment.	
Regulations and guidelines	FTAC 1	Create a mechanism for registered entities to request SAR interpretations.	A mechanism for registered entities to request SAR interpretations has been developed and is available for access on the FSAP website.	
Regulations and guidelines	FTAC 4	Ensure that individuals with BSAT access can transfer access to another registered entity without the need to reapply.	A mechanism for individuals with BSAT access to transfer their access to another registered entity was implemented in July 2016.	
Regulations and guidelines	FTAC 5	Develop a process to relax FSAP requirements quickly in emergency situations.	Language addressing the expedited SRAs for approval to work with BSAT was present in 42 CFR 73 section 73.10(f) before this recommendation, and government health officials claim that current emergency waiver authorities are sufficient for anticipated needs. However, no additional public steps were taken to verify sufficiency.	
Regulations and guidelines	FTAC 13	Develop a BSAT training program for customs inspectors.	A BSAT training program for customs inspectors was developed and implemented in January 2016.	

Necessary number of high-containment laboratories in the United States	FESAP	Perform a Federal assessment of high-containment needs for protecting against emerging infectious disease while minimizing unintentional laboratory release risk.	A Federal assessment of high-containment needs in the United States was performed.	
Necessary number of high-containment laboratories in the United States	FESAP	Perform an external assessment of high-containment needs for protecting against emerging infectious disease while minimizing unintentional laboratory release risk.	No information on an external assessment of high-containment needs in the United States is available. A sufficient assessment of high-containment needs is crucial for pandemic preparedness due to the large amount of time and money involved in developing high-containment facilities.	
Necessary number of high-containment laboratories in the United States	FESAP	Consolidate and review the recommendations made from the Federal and external assessments of high-containment needs in the United States.	No information on a consolidation and review of Federal and external assessments of high-containment needs in the United States is available. A sufficient assessment of high-containment needs is crucial for pandemic preparedness due to the large amount of time and money involved in developing high-containment facilities.	
Necessary number of high-containment laboratories in the United States	FESAP	Develop a best practices checklist for use by registered entities when considering modifications to containment capacity.	A best practices checklist for use by registered entities when considering modifications to containment capacity was developed as a result of the Federal high-containment needs assessment.	

Conclusion

- 33 actions recommended
  - 16 addressed
  - 11 insufficiently addressed
  - 6 not addressed
- Important next steps
  - Determine if US has enough high-containment lab space
  - Develop and implement applied biosafety research program
  - Develop an engaging bioethics training program
  - Develop an Aviation Safety Reporting System-like BSAT incident reporting system

Discussion

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