U.S. Government's Policy for Oversight of Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential: A Discussion

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Huge thank you to Rebecca Moritz, for letting me borrow (steal) some slides!
Thank you to David Gillum, for the most awesome timeline ever!

Framing the Discussion

- I am anticipating some of this group is familiar with the following:
  - United States Government Policy for Oversight of Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential
  - IMPLEMENTATION GUIDANCE for the United States Government Policy for Oversight of Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential
  - Previous DURC policy
  - Federal Select Agent Program and its oversight
- However, I will begin with some background to level the field. Please stop me if you have questions or I use an acronym you are unfamiliar with.
- I am speaking from the perspective of a EHS Executive Director, biosafety/biosecurity professional, IBC administrator, PI, and ABSA International President that has enough information about the new policies to be dangerous.
- I fully expect to learn as much as I share.
- This is going to go fast. Buckle up.

How Did We Get Here?
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- When was the NIH Recombinant Advisory Committee (RAC) formed?

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  October 7, 1974

How Did We Get Here?

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- When was the NIH Recombinant Advisory Committee (RAC) formed?
  October 7, 1974
  - 2024-1974 = ??? years

How Did We Get Here?

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- When was the NIH Recombinant Advisory Committee (RAC) formed? October 7, 1974
- What happened February 24-27, 1975?

How Did We Get Here?

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- When was the NIH Recombinant Advisory Committee (RAC) formed? October 7, 1974
- What happened February 24-27, 1975? Asilomar Conference
- When did we see the first rDNA Guidelines?

How Did We Get Here?

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- When was the NIH Recombinant Advisory Committee (RAC) formed? October 7, 1974
- What happened February 24-27, 1975? Asilomar Conference
- When did we see the first rDNA Guidelines? July 23, 1976
- November 1983: WHO publishes first biosafety manual. May 1984: First edition of CDC/NIH BMBL published. What happened between these dates?
  - Hint – it's not good…

How Did We Get Here?

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- When was the NIH Recombinant Advisory Committee (RAC) formed? October 7, 1974
- What happened February 24-27, 1975? Asilomar Conference
- When did we see the first rDNA Guidelines? July 23, 1976
- November 1983: WHO publishes first biosafety manual. May 1984: First edition of CDC/NIH BMBL published. What happened between these dates? September 1984: First bioterrorist attack in the U.S. The Rajneeshee commune in Oregon used Salmonella to contaminate salad bars sickening over 750 people.

How Did We Get Here?

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- When was ABSA founded?

How Did We Get Here?

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- When was ABSA founded? June, 1984

How Did We Get Here?

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- When was ABSA founded? **June, 1984**

  2024 – 1984 = ??? years

How Did We Get Here?

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- When was ABSA founded? **June, 1984**
- **April 24, 1996**: Passage of first law controlling certain biological agents. Passage of the **Antiterrorism and Effective Death Penalty Act of 1996 (PL 104-132)**, authorizing the Secretary of Health and Human Services to establish regulatory control over transfers, but not possession or use, of listed biological agents.
- **June 10, 1996: First Select Agent regulations.** CDC published the "Notice of Proposed Rulemaking (NPRM) to Implement Section 511 of Public Law 104-132, 'The Antiterrorism and Effective Death Penalty Act of 1996'."
- **October 24, 1996:** Regulations for Transferring Select Agents. "**Additional Requirements for Facilities Transferring or Receiving Select Agents**" (42 CFR Part 72.6) enters into force.

How Did We Get Here?

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- Fall 2001: What happened?
  - Really not good…more than one answer…

How Did We Get Here?

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- Fall 2001: 9/11. Then Amerithrax attacks. In October 2001, an American Media Inc. (AMI) employee in Florida was diagnosed with inhalational anthrax, the first U.S. case in over two decades. By November 2001, 21 additional cases and 5 deaths occurred, and by December 2001, the EPA confirmed anthrax contamination at over 60 sites, including numerous postal facilities.

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- **What was the response?**

How Did We Get Here?

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- **What was the response?** October 26, 2001: **USA PATRIOT Act.** This law builds on the then-existing Select Agent regulations by prohibiting "restricted persons" from possessing them.

How Did We Get Here?

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- June 12, 2002: Public Health Security and Bioterrorism Preparedness and Response Act of 2002, which extended the biological select agents and toxins program by calling for the Secretaries of Agriculture and HHS to establish a system to regulate possession of these agents by banning their transfer to or possession by any **individuals or entities not registered to have them.**
- December 13, 2002: The Federal Select Agent Program is expanded to oversee the possession, use, and transfer of biological select agents and toxins that pose a severe threat to public health and safety.
- February 2003: Biodefense and biosecurity statement. Publications by Nature, Science, and Proceedings of the National Academy of Sciences of Statement on the Consideration of Biodefense and Biosecurity by a group of scientific journal editors, scientist-authors, government officials, and others, which among other things states that, "We recognize that on occasions **an editor** may conclude that the potential harm of publication outweighs the potential societal benefits. Under such circumstances, the paper should be modified, or not be published." [This followed from a meeting held on January 10, 2003, the day after a joint National Academies/Center for Strategic and International Studies conference on scientific openness and national security]
- October 18, 2003: Release of the National Academies' report **Biotechnology Research in an Age of Terrorism** –I dentified seven classes of experiments of concern that warrant review and discussion before being conducted and recommended formation of a National Science Advisory Board for Biodefense (later enacted, with some changes, as the National Science Advisory Board for Biosecurity).
  - Bonus points – what is this report commonly called?

How Did We Get Here?

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- March 4, 2004: Formation of the **NSABB**. The National Science Advisory Board for Biosecurity (NSABB) is established in the USA to advise on dual-use research issues. One of its early tasks includes reviewing the controversial reconstruction of the 1918 influenza virus.
- June 30-31, 2005: Inaugural NSABB meeting to discuss the oversight of dual-use research and related biosecurity issues.
- June 2007: The NSABB publishes a report outlining a framework for the oversight of life sciences research that could be of concern for dual-use purposes.

- 2007-2004 = ?? years

How Did We Get Here?

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- October 4, 2007: HHS establishes a Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight.
- January 9, 2009: President Obama signs Executive Order 13486, focusing on strengthening laboratory biosecurity measures to protect against biological threats.
- July 2, 2010: ????? established.

How Did We Get Here?

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- October 4, 2007: HHS establishes a Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight.
- January 9, 2009: President Obama signs Executive Order 13486, focusing on strengthening laboratory biosecurity measures to protect against biological threats.
- July 2, 2010: Federal Experts Security Advisory Panel - **FESAP established**. EO 13546 - tightened the Select Agent regulations and established FESAP, called for a tiering of the select agent list to provide additional security for those presenting the greatest risk of misuse.

How Did We Get Here?

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- October 13, 2010: USG issues guidance for the **screening of synthetic double-stranded DNA** to prevent its misuse for bioterrorism or other malicious purposes. (Commercial providers)

- Winter 2011/Spring 2012: NSABB Reviews of Controversial H5N1 Research. The NSABB meets on December 15, 2011 and March 29-30, 2012 to review research by Yoshi Kawaoka and Ron Fouchier that demonstrates that the H5N1 influenza virus can become transmissible in mammals. The **NSABB recommends publication despite biosecurity concerns**, leading to significant debate within the scientific community about the risks and benefits of such research.

How Did We Get Here? First time DURC shows up!

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- March 29, 2012: "United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern (DURC)," which requires the review of **U.S. government-funded research involving 15 specific agents and toxins and 7 categories of experiments**. The policy mandates the development of risk mitigation plans for experiments identified as Dual Use Research of Concern.
- February 21, 2013: HHS of "A Framework for Guiding U.S. Department of Health and Human Services Funding Decisions about Research Proposals with the Potential for Generating Highly Pathogenic Avian Influenza H5N1 Viruses that are Transmissible among Mammals by Respiratory Droplets"
  - August 7, 2013: H7N9 announcement. Announcement of extra oversight for H7N9 experiments (along the lines of the reviews previously issued for certain H5N1 experiments).
- September 24, 2014: **Institutional Oversight Policy for DURC.**

2014-2012 = ??? years

How Did We Get Here? 10 years to go…

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- October 17, 2014: U.S. Moratorium on GOF Research. NIH imposes a moratorium on gain-of-function (GOF) research involving PPPs, including influenza, SARS-CoV, and MERS-CoV, due to biosecurity and biosafety concerns following a series of biosafety lapses at US government laboratories.
- December 2014: FESAP issued a report titled "Recommendations for the Evaluation and Oversight of Gain-of-Function Research." The report provides comprehensive recommendations for strengthening the oversight and management of gain-of-function research involving potentially pandemic pathogens, emphasizing the need for enhanced biosafety and biosecurity measures.
- December 15-16, 2014: The U.S. National Academy of Sciences holds symposium "Gain-of-Function Research: A Symposium"
- April 13, 2015: The National Academies Press publishes "Potential Risks and Benefits of Gain-of-Function Research: Summary of a Workshop," discussing the ethical and practical implications of GOF research with pathogens of pandemic potential.
- May 2015: NSABB issues a framework for conducting risk and benefit assessment of gain-of-function research
- March 10-11, 2016: The National Academies holds a symposium "Gain-of-Function—The Second Symposium".
- April 2016: Gryphon Scientific publishes Risk and Benefit Analysis of Gain of Function Research, Final Report-April 2016.
- May 2016: The NSABB publishes recommendations for the evaluation and oversight of gain-of-function research, emphasizing the need for robust risk assessment and management strategies.
- June 20, 2016: A publication of National Academies of Sciences, Engineering, and Medicine regarding their 2nd workshop.
- **January 9, 2017: The OSTP releases the "Recommended Policy Guidance for Departmental Development of Review Mechanisms for Potential Pandemic Pathogen Care and Oversight" (P3CO), establishing additional review processes for GOF research involving PPPs.**
- **December 19, 2017: HHS releases "Framework for Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens," which implements the OSTP P3CO Framework and lifts the moratorium on funding gain-of-function.**
- July 2018: Follow-up on GOF research. Two research projects that were paused in 2014 are reviewed and approved under the new P3CO policy, allowing them to continue. These projects conclude in 2019.

GoF

How Did We Get Here? 10 years to go…

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- **January 9, 2017: P3CO policy guidance. The OSTP releases the "Recommended Policy Guidance for Departmental Development of Review Mechanisms for Potential Pandemic Pathogen Care and Oversight" (P3CO), establishing additional review processes for GOF research involving PPPs.**
- **December 19, 2017: Implementation of P3CO Framework. HHS releases "Framework for Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens," which implements the OSTP P3CO Framework and lifts the moratorium on funding gain-of-function. s**
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How Did We Get Here?

2019 - COVID.

Top secret Wuhan lab leak intel may finally be released if Trump wins election & give world answers, ex-CDC chief says | The Sun

Summary Before We Continue:

- Where did term DURC come from?
  - Dual Use Research of Concern
- 2012 – USG Policy for Life Sciences DURC
- 2014 – USG Policy for Oversight of Life Sciences DURC
  - List based oversight of 15 agents and 7 experimental outcomes of concern
  - Expanded the framework for oversight
    - ICDUR and IRE established
    - NSABB established
  - Defined the roles and responsibilities of PIs, institution, and USG funding agencies.

Will the intermediate or final products of your research:

1. Enhance the harmful consequences of the agent or toxin?
2. Disrupt immunity or the effectiveness of an immunization against the agent or toxin?
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?
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 or will synthetic biology techniques be used to construct a pathogen, toxin, or potentially harmful product?

15 Agents

Avian influenza virus (highly pathogenic), *Bacillus* anthracis, Botulinum neurotoxin (in any quantity), *Burkholderia mallei, Burkholderia pseudomallei,* Ebola virus, Foot-and-mouth disease virus, *Francisella tularensis,* Marburg virus, Reconstructed 1918 influenza virus, Rinderpest virus, Toxin-producing strains of Clostridium botulinum, Variola major virus, Variola minor virus, *Yersinia pestis*

United States Government Policy for Oversight of Dual Use Research of Concern and Pathogens of Enhanced Pandemic Potential – May 2024

United States Government Policy for Oversight

New DURC and PEPP Policy

Provides a unified oversight framework for Dual Use Research of Concern (DURC) and Pathogens with pandemic potential (PPP)

Goes into effect May 2025

Supersedes

- 2012 USG Policy for Oversight of Life Sciences Dual Use Research of Concern
- 2014 USG Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern
- 2017 Recommended Policy Guidance for Departmental Development of Review Mechanisms for Potential Pandemic Pathogen Care and Oversight (P3CO)

New Definitions

- **Dual use research of concern (DURC)** is life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be misapplied to do harm with no, or only minor, modification to pose a significant threat with potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security
- **Pathogen with pandemic potential (PPP)** is a pathogen that is likely capable of wide and uncontrollable spread in a human population and would likely cause moderate to severe disease and/or mortality in humans
- **Pathogen with enhanced pandemic potential (PEPP)** is a type of pathogen with pandemic potential (PPP) resulting from experiments that enhance a pathogen's transmissibility or virulence, or disrupt the effectiveness of pre-existing immunity, regardless of its progenitor agent, such that it may pose a significant threat to public health, the capacity of health systems to function, or national security. Wild-type pathogens that are circulating in or have been recovered from nature are not PEPPs but may be considered PPPs because of their pandemic potential.

Category 1 Research

- Meets three criteria:
  - Involves one or more of the biological agents and toxins specified in the policy
  - Is reasonably anticipated to result, or does result, in one of the experimental outcomes specified in the policy
  - Based on current understanding, the research institution and/or federal funding agency assesses that the research constitutes DURC as specified in the policy

Category 1 Biological Agents and Toxins

- All Select Agents and Toxins listed in 9 CFR 121, 42 CFR 73, and 7 CFR 331 and regulated by USDA and/or HHS
- All Risk Group 4 pathogens listed in Appendix B of the NIH Guidelines- Classification of Human Etiologic Agents on the Basis of Hazard
- A subset of Risk Group 3 pathogens listed in Appendix B of the NIH Guidelines
- Agents affecting humans, not assigned a Risk Group in the NIH Guidelines, but recommended by BMBL to be handled at BSL-3 or BSL-4
- Agents added during future updates

Category 1 Experimental Outcomes

1. Increase transmissibility of a pathogen within or between host species
2. Increase the virulence of a pathogen or convey virulence to a non-pathogen
3. Increase the toxicity of a known toxin or produce a novel toxin
4. Increase the stability of a pathogen or toxin in the environment, or increase the ability to disseminate a pathogen or toxin
5. Alter the host range or tropism of a pathogen or toxin
6. Decrease the ability for a human or veterinary pathogen or toxin to be detected using standard diagnostic or analytical methods
7. Increase resistance of a pathogen or toxin to clinical and/or veterinary prophylactic or therapeutic interventions
8. Alter a human or veterinary pathogen or toxin to disrupt the effectiveness of preexisting immunity, via immunization or natural infection, against the pathogen or toxin
9. Enhance the susceptibility of a host population to a pathogen or toxin

Compare…

DURC

1. Enhance the harmful consequences of the agent or toxin?
2. Disrupt immunity or the effectiveness of an immunization against the agent or toxin?
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?
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 or will synthetic biology techniques be used to construct a pathogen, toxin, or potentially harmful product?

Category 1

1. Increase transmissibility of a pathogen within or between host species
2. Increase the virulence of a pathogen or convey virulence to a non-pathogen
3. Increase the toxicity of a known toxin or produce a novel toxin
4. Increase the stability of a pathogen or toxin in the environment, or increase the ability to disseminate a pathogen or toxin
5. Alter the host range or tropism of a pathogen or toxin
6. Decrease the ability for a human or veterinary pathogen or toxin to be detected using standard diagnostic or analytical methods
7. Increase resistance of a pathogen or toxin to clinical and/or veterinary prophylactic or therapeutic interventions
8. Alter a human or veterinary pathogen or toxin to disrupt the effectiveness of preexisting immunity, via immunization or natural infection, against the pathogen or toxin
9. Enhance the susceptibility of a host population to a pathogen or toxin

Category 1 Risk Assessment

Based on *current* understanding, the research can be *reasonably* anticipated to provide, or does provide, knowledge, information, products, or technologies that could be misapplied to *do harm* with *no — or only minor — modification* to pose a *significant* threat with potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security

HOWEVER……

- There maybe additional types of life science research that does not include these agents or experiments that could pose DURC risks
- Encouraged to include work involving any other biological agent or toxin regardless of its Risk Group and develop and apply appropriate risk mitigation

Category 2 Research

- Meets three criteria:
  - Involves, or is reasonably anticipated to result in, a PPP as specified in the policy
  - Is reasonably anticipated to result in, or does result in, one or more of the experimental outcomes or actions specified in the policy
  - Based on current understanding, the research institution and/or federal funding agency assesses that the research is reasonably anticipated to result in the development, use, or transfer of a PEPP or an eradicated or extinct PPP that may pose a significant threat to public health, the capacity of health systems to function, or national security as specified in the policy

Category 2 Biological Agents

- A PPP, or any pathogen that will be modified in such a way that is reasonably anticipated to result in a PPP

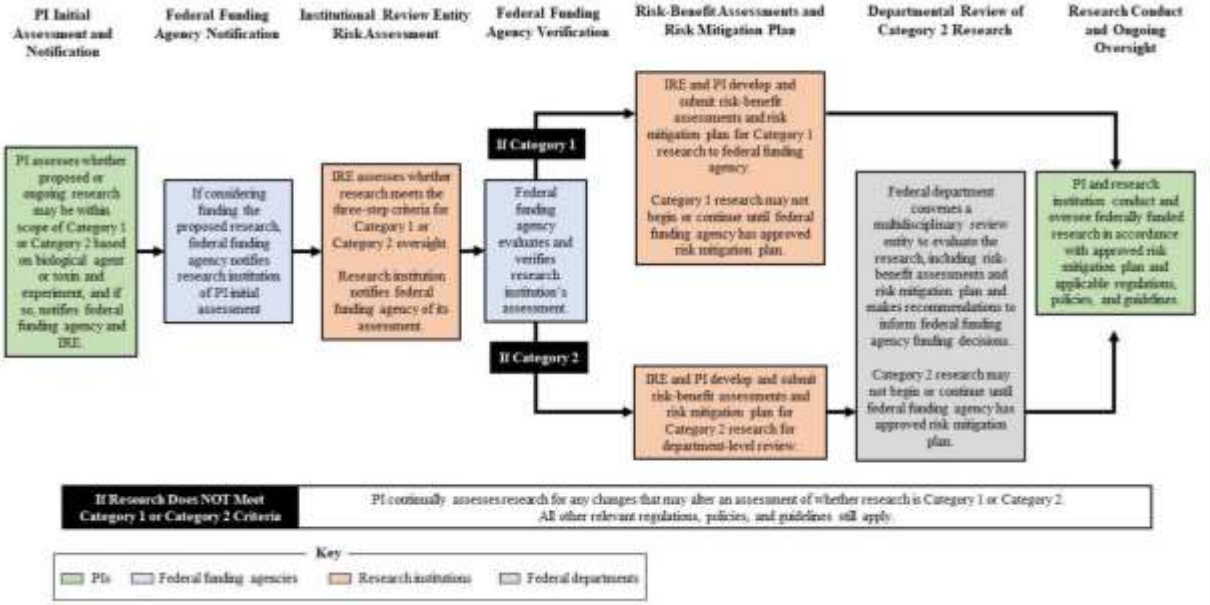
Category 2 Experimental Outcomes or Actions

1. Enhance transmissibility of the pathogen in humans
2. Enhance the virulence of the pathogen in humans
3. Enhance the immune evasion of the pathogen in humans such as by modifying the pathogen to disrupt the effectiveness of pre-existing immunity via immunization or natural infection
4. Generate, use, reconstitute, or transfer an eradicated or extinct PPP, or a previously identified PEPP

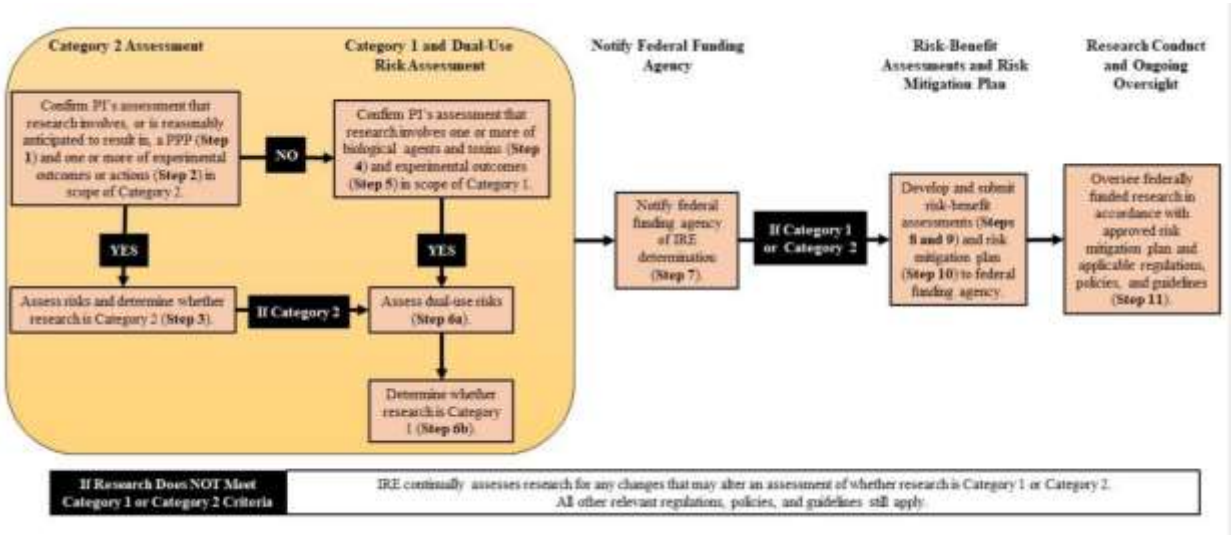
Category 2 Risk Assessment

The research can be reasonably anticipated to result in the development, use, or transfer of a PEPP or an eradicated or extinct PPP that may pose a significant threat to public health, the capacity of health systems to function, or national security

Overview of Review Process for Category 1 or Category 2 Research



IRE Review Process for Category 1 and Category 2 Research



Ongoing IRE Oversight/Review

- Continually assess research for any changes that may alter a Category 1 or Category 2 assessment
- Annually review Category 1 risk mitigation plans (this could extend to progress reviews)
- Semi-annually review Category 2 risk mitigations plans (this could extend to progress reviews)

Additional Entity Duties

- Responsible for ensuring that PIs are aware of and executing the responsibility to do an initial assessment of their research and notifying the funder and IRE
- Ensure research meeting the scope for Category 1 will not proceed until the funder approves the risk mitigation plan
- Ensure research meeting the scope for Category 2 will not proceed until the funder determine the potential benefits and justifies the potential risk and approves the risk mitigation plan
- Ensure research that is identified as potentially falling within the scope of Category 1 or 2 during the course of experimentation, is halted by the PI and the PI notifies the funder and IRE
- Ensure responsible communication of research results
- IRE policies must be publicly available
- Report instances of failure to follow the policy within 30 calendar days
- Annually provide formal assurance to relevant federal funding agencies

Research Institutions are encouraged to expand their oversight and apply these mechanisms for other life sciences research, and research in other field converge with biology, when appropriate; however, any such expansion would not be subject to oversight requirements articulated in the Policy

Yet….voluntary guidance says an entity should update federal finding agencies if unexpected Category 1 or 2 research is identified for any human or zoonotic biological agent or toxin

Here to help!

IMPLEMENTATION GUIDANCE
for the
United States Government Policy for Oversight of Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential

May 2024

Type of Misuse

- In what ways could the knowledge, information, products, or technologies from the research be misused?
- The risk of misuse may be higher for research that can be directly misused than for research that requires significant additional scientific advances to facilitate its misapplication.
- What types of knowledge, information, products, or technologies are anticipated to be generated through the research?
- Can the knowledge, information, products, or technologies from the research be misapplied with no, or only minor, modification to cause harm?
- If not, do the outcomes of the research need to be combined with other knowledge, information, products, or technologies in order to pose a threat?
- If so, is the other knowledge, information, products, or technologies already or readily available?
- Is there concern about immediate or near-future potential misuse, or is the concern about misuse in the distant future?
- Consider the time frame in which information from the research might be misused. Information that can be misused in the near term may be of greater concern.

Ease of Misuse

- How easily could the knowledge, information, products, or technologies be misapplied to do harm with no, or only minor, modification?
- Consider the technical expertise and/or physical resources that would be required to apply the knowledge, information, products, or technologies for malevolent purposes.
- The risk of misuse may be lower for knowledge, information, products, or technologies that would be expensive, difficult to procure, or that require a high degree of technical skill to facilitate such misuse.
- Would misuse of the knowledge, information, products, or technologies require a low or high degree of technical skill and sophistication to use the information from dual use research for harmful purposes?
- Alternatively, would it make achieving the harmful outcome easier for an unsophisticated actor?
- Would misuse of the knowledge, information, products, or technologies require materials, equipment, or reagents that are expensive or difficult to procure?

Dissemination

- How will the knowledge, information, products, or technologies of the research in question be shared or distributed?
- Knowledge, information, products, or technologies that are freely available and widely distributed may be more easily accessed by individuals with harmful intent.
- Who will have access to the knowledge, information, products, or technologies?
- Will the knowledge, information, products, or technologies be shared openly or remain within the laboratory?

Information Risks

- What is the novelty of the information provided by the research or research methods?
- Research that adds novel information or consolidates information in novel ways may be of greater concern than information that is already widely available.
- Have the results of similar research been previously described or shared?
- If so, at what venues and in what detail?
- How readily available are these results?

Potential Vulnerabilities

- Does the research highlight vulnerabilities or consolidate existing information in ways that highlight vulnerabilities in existing MCMs, public health approaches, or agricultural infrastructure?
- Research that highlights vulnerabilities could impede our ability to prepare for and respond to disease outbreaks that could impact public health, agriculture, food security, economic security, or national security.

Potential Consequences

- How readily could the knowledge, information, products, or technologies from the research be used to threaten public health, agriculture, food security, economic security, or national security?
- Think broadly about the potential impacts on public health, agriculture, food security, economic security, or national security from the intentional misapplication of the results from the research in question. In general, information that could be misused to harm large populations of humans, plants, or animals; cause public panic; or require costly response efforts would be considered a greater risk.
- Consider the nature of the potential consequences that might result from misuse of the research results in question. Information that could be misused to harm numerous sectors of society or the environment may be of greater concern.
- Consider the scope and magnitude of the potential consequences. Research or research information that could be misused to cause severe harm, disease, or consequences is generally considered to be of greater concern. Could the impact on people, animals, and/or plants be considered minor, moderate, or major?
- Consider the availability and efficacy of MCMs. Sufficient and efficacious MCMs could decrease concern about the consequences of misuse. MCMs may include drugs, biological products, public health practices, pesticides, or devices intended for diagnosis, detection, mitigation, prevention, or treatment.
- Are there currently any MCMs to help mitigate the potential consequences of misuse?
- Are the MCMs readily and widely available?
- What are the impacts on the healthcare system when it comes to administering the MCMs?

Benefits

- What are the potential benefits to public health, agriculture, food security, economic security, or national security from the research?
- What potential solution(s) does the research offer to an identified problem or vulnerability?
- How would the research be useful to the scientific, public health, national security, or agriculture communities?
- How will the knowledge, information, technology, or products generated from the research be broadly applicable (e.g., to human health, multiple scientific fields, populations of organisms)?
- If a benefit has been identified, in what time frame (e.g., immediate, near future, years from now) might this research benefit public health, agriculture, food security, economic security, or national security?

Benefits vs Risks

- Are there other ways in which the potential benefits of the research could be achieved that would reduce the anticipated risks?
- Could the knowledge, information, products, or technologies of concern be more readily applied to improvements in surveillance, development of MCMs, or other beneficial purposes than to malevolent applications? What reasons or evidence support the answer to this question?
- What is the time frame in which potential benefits might be realized? Does it rely on other research endeavors?
- How might the potential benefits and the anticipated risks be distributed across different human, animal, and plant communities? Who or what will be the likely beneficiaries of the potential benefits? Who or what will bear the anticipated risks? Is it likely that one or more specific populations will bear the burden of the anticipated risks?
- Considering the anticipated risks along with potential benefits, are the risks of such a feasibility and magnitude that they warrant proceeding after developing and implementing a risk mitigation plan? Are the potential benefits of significant magnitude to warrant proceeding despite the risks?
- What is the most responsible way to proceed? Do measures in the risk mitigation plan effectively and measurably reduce the anticipated risk?

Strategies for Mitigation Risk Already in Place

- When applicable, select agent regulations
- Terms and conditions of the grant or contract for NIH Guidelines, BMBL, and requirement to work at a certain BSL
- *NIH Guidelines* require that the biosafety aspects of the research be reviewed and approved (where appropriate) by an IBC
- Research has been reviewed for its Category 1 or Category 2 potential by an appropriately constituted IRE
- PI and researchers are required by the terms and conditions of the grant or contract to undergo training in the safe conduct of research
- A designated management plan for the full life-cycle for the research
- Required by the grant or contract to undergo training in the responsible conduct of research and/or research ethics as required by the institution and federal guidelines
- Required by the grant or contract to be enrolled in an occupational health surveillance program, when appropriate

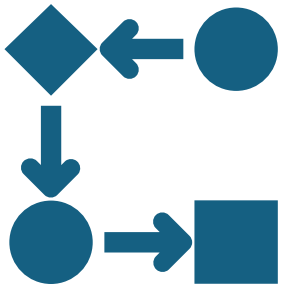
New Risk Mitigation Strategies

- Modify the design or conduct of the research to mitigate potential risks while achieving the benefits
- Apply specific or enhanced biosafety and biosecurity measures
- Evaluate MCM efficacy against biological agents or toxins
- Refer the institution to available educational tools for assessing and mitigating potential risks of the research
- Regularly review, at the institutional level, emerging research findings for additional Category 1 and Category 2 research
- Request that institutions notify federal funding agencies if additional Category 1 or Category 2 research is identified, and propose modifications to the risk mitigation plan, as needed
- Determine the venue and mode of to communicate the research responsibly
- Review annual progress reports from PIs to determine if Category 1 and Category 2 research results have been generated
- Develop a plan and methodologies for responsibly communicating the findings of the research, any time during the lifecycle of the project, including voluntary redaction of the research publications or communications

So Let's Talk...

Where Do We Start?

- Lots of feelings about this policy…
- Lots of “I heard”, “what if”, and “what does that mean” going on…
- How do we collect it all?
  - Logistics
  - Technology
  - Cost / Staffing
  - Training / Resources
  - Unintended Consequences
  - Timing



Logistics

- Scope
  - strongly encourages non-federally funded work to comply.
  - strongly encourages all work outside Category 1 and Category 2 be assessed. Concerned entity leadership may want to overprotect and require all recombinant and BSL-2 work be included.
- Will current research be paused? Unclear.
- How many protocols will be covered? Unclear.
- Entity IRE will now need to review pre-award. The IBC or safety office does not generally review proposals. The concern is that significant effort will go into reviewing pre-award proposals that will not receive funding. This reduces resources for oversight of funded research. Could lead to EHS/IBC being seen as a barrier to grant submittal process.
- Will entities have a “file manager” as in FSAP to streamline communication and assist with process? Concerned the PI is on their own until research is deemed “eligible for federal funding”.

Technology

How are assessments being submitted to the agencies?

Some entities use cloud-based research management systems and some are in word/pdf documents.

The implementation guidance has terms like “Select all applicable additional measures from this menu to summarize the risk mitigation measures”. Does this imply there is a tool that all entities will use to allow for consistency and efficiency? Will this track progress through the process? Can the entity monitor the process? When will the tool become available?

Will communication between entities and agencies be managed within such a tool to ensure continuity? (ex. FSAP portal)

Cost/Staffing

- Public institutions are stressed and contracting budgets.
- Entities cannot provide cost estimate for compliance, since parameters are unclear.
- However, it is understood that:
  - Pre-award review is not currently common practice;
  - Role of ICDUR may be enhanced;
  - If the IRE is separate from IBC, entity compliance administration (biosafety officer, compliance manager) will need to manage a new committee;
  - If IRE is IBC, IBC will see increased workload
    - IBCs are becoming difficult to staff and engage
  - Administrative support staff will be needed to track status and manage communication.
    - Many IBC do not have the coordinator or analyst positions the IRB and IACUC may have.

Training / Resources

Concerned that entities are deemed responsible for developing training on the policy. For consistency, OSTP should provide the training materials for entities to incorporate into their site-specific offerings.

Concerned the policy has not been finalized, and submission tools not available, for entities to train PI and admin staff on before May 2025.

Unintended Consequences

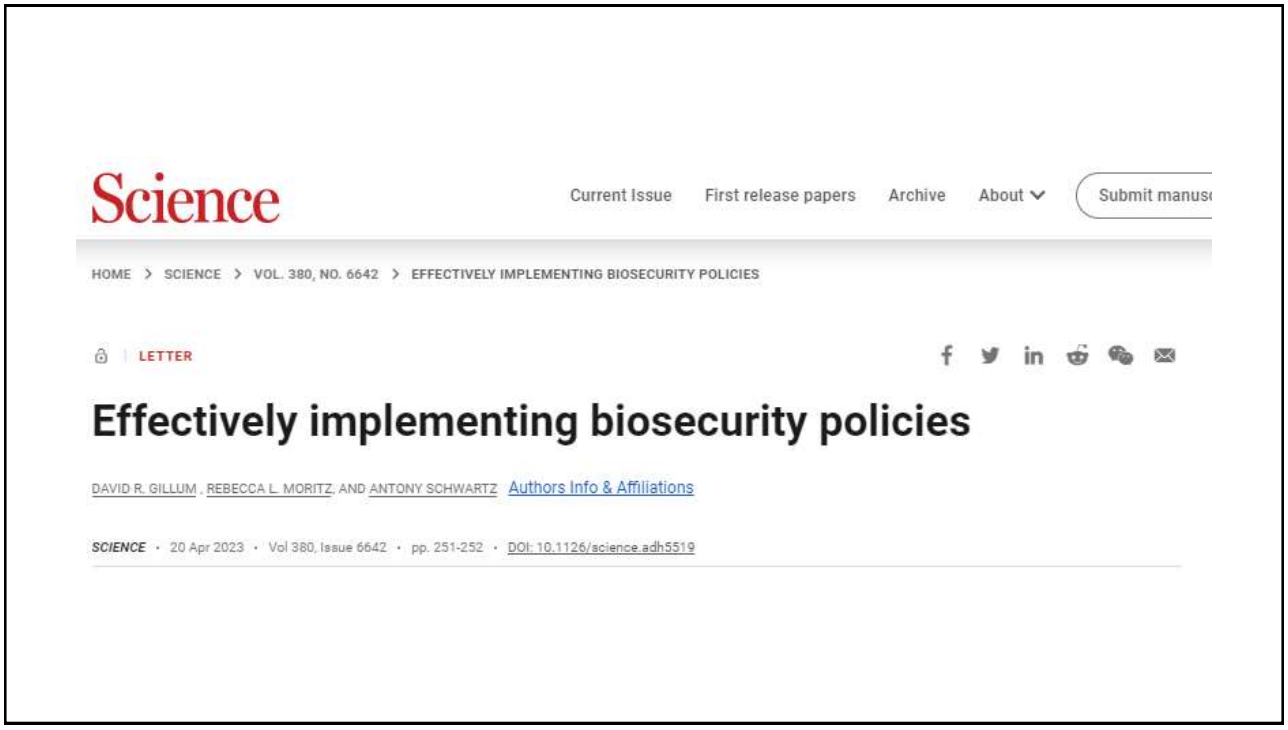
- Research on important topics becomes “too hard” to do
- Researchers leaving entities because they do not feel supported
- Critical work is paused (ex. GOF pause that interrupted St. Jude annual flu vaccine development)

Timing

- OSTP holds entities to timeframes, but no timeframes proposed related to ensuring agency review is timely.
- Policy states entities need to be compliant by May 2025, but we have heard NIH will go first and others should follow their process?
- Dr. Lauer stated that OSTP expects it to take 2-3 cycles to perfect the process.
- Entities cannot be training PIs and admin staff now if the process has not been solidified.
- Entities cannot propose budget to hire new staff and train them by May 2025 as we cannot predict scope or burden.

What Does the Future Hold?

- Sen. Rand Paul (R-Ky.) has introduced the Risky Research Review Act (S. 4667)
  - Proposes a Life Sciences Research Security Board that reviews federally funded life sciences research involving "high-risk" experiments and to decide if such research should be funded.
    - Board would have the ability to veto research, even if not deemed "high risk"
    - definition of high-risk life sciences research is broad and ambiguous
    - covers BSAT and DURC and reaches beyond the expansion of DURC and PEPP discussed here
      - includes pathogen collection and surveillance
      - covers — any research that "could pose a threat to public health, safety, or national security."
        - would include: vaccine research and development, characterizing known and emerging pathogens, pandemic preparation, novel therapeutics



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LETTER

Effectively implementing biosecurity policies

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What Can ABSA International Do?

- **Engage our membership**
  - Surveys
  - Community of practice to support members in implementing the process
  - Collect experiences
- **Provide comments** – Technical and Legislative Regulatory Review Committee
  - Develop and implement an effective method for reviewing and commenting on issues or regulatory concerns that impact the ABSA membership or the health or safety of the environment. Respond to requests for comments by regulatory agencies proposing new or amended regulations. Develop "white papers" and other guidance documents.
- **Training Vehicle**
  - Webinars – can be collaboration with OSTP and/or regulated entities
  - Pre-Conference course
  - Affiliate meetings – often co-hosted (ex. ABSA and ASM local chapters can partner to hold meeting)
- **Provide Resources**
  - Recorded training, useful links, lessons learned
  - *Applied Biosafety*
- **Partner!**

Selected References

- Risky Research Review Act (S. 4667)
- Gillum, D. R. Balancing Innovation and Safety: Frameworks and Considerations for the Governance of Dual-Use Research of Concern and Potential Pandemic Pathogens. **Applied Biosafety.** 2024.https://doi.org/10.1089/apb.2024.00
- Gillum D, Moritz R, Koblentz GD. The "risky research review act" Would do more harm than good. **STAT**. 2024 Jul 19. Available from: https://www.statnews.com/2024/07/19/risky-research-review-act-more-harm-than-good/ [Last accessed: November 11, 2024].