National Institutes of Health

Office of Science Policy

Dual Use and Gain-of-Function Research Oversight Policy

Carrie D. Wolinetz, Ph.D.

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Promoting Health Security through Life Sciences Research

- Robust life sciences research enterprise critical to promoting public health and well-being, particularly in light of evolving threats posed by microbial pathogens
- USG supports a diverse life sciences research portfolio
- Research involving potentially dangerous pathogens has inherent biosafety and biosecurity risks
- *Key challenge:* How to facilitate beneficial biological research while mitigating risks of misuse?

Safely realizing the benefits of pathogen research requires effective:

- ✓ Risk assessment and risk mitigation
- ✓ Policies, practices, and oversight

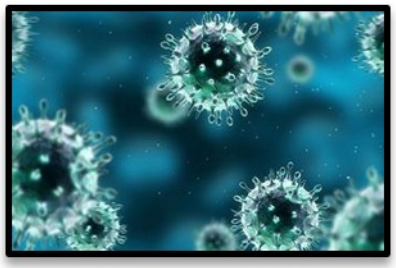
Biosafety & Biosecurity: Federal Policies and Guidelines

- **Comprehensive oversight framework includes:**
  - **Occupational Health and Safety Regulations & Standards**
  - **Biosafety in Microbiological and Biomedical Laboratories (BMBL)**
  - ***NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules***
  - **Select Agent Regulations**
  - **Screening Framework Guidance for Providers of Synthetic Double-Stranded DNA**
  - **Dual Use Research of Concern (DURC) Policies**
  - **Potential Pandemic Pathogen Care and Oversight (P3CO) - USG Policy & HHS Framework**

Dual Use Research of Concern

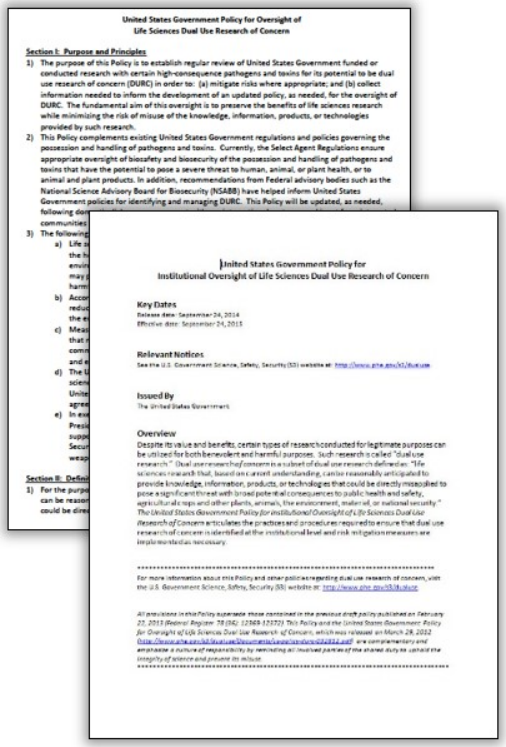
- Dual use research (DUR): Life sciences research that has the potential to be utilized both for benevolent and harmful purposes

- Dual Use Research of Concern (DURC): Subset of research that has the greatest potential to generate knowledge, information, or products that could be readily misused to pose significant threat to public health and national security



U.S. Government DURC Policies

- **Two USG policies for the oversight of dual use research of concern (DURC)**
  - ***USG Policy for Oversight of Life Sciences DURC***
    Requires federal funding agencies to identify DURC in their research portfolios and work to mitigate risks as needed
  - ***USG Policy for Institutional Oversight of Life Sciences DURC***
    Requires federally-funded research institutions to establish a system to identify DURC and work with funding agencies to mitigate risks as needed


United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern

Section I: Purpose and Principles

United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern

Key Dates

Relevant Notices

Issued By

Overview

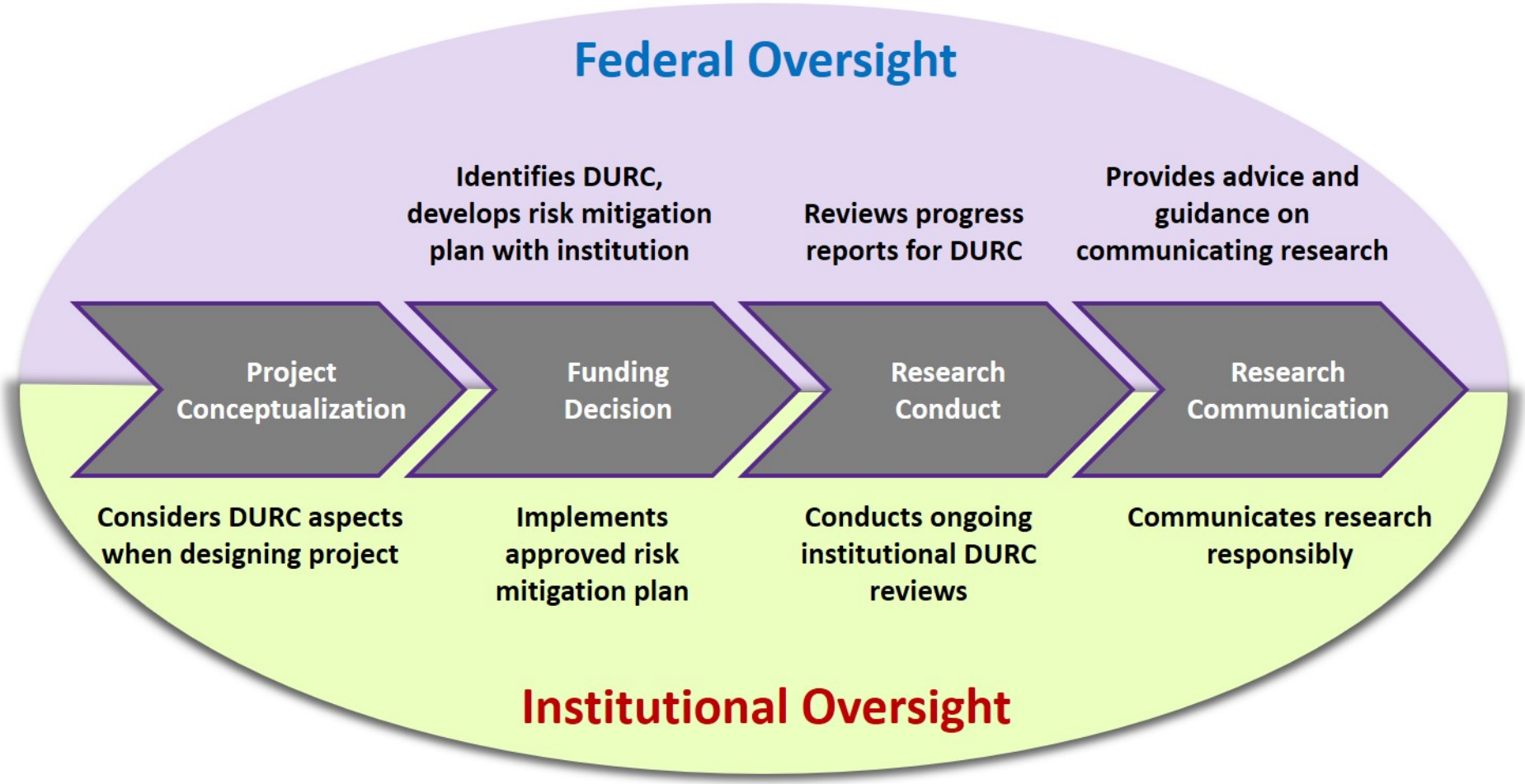
www.phe.gov/s3/dualuse

U.S. Government DURC Policies: Purpose and Principles

Aim to preserve the benefits of life sciences research while minimizing the risk of misuse of the information, products, or technologies generated by such research

- Free and open conduct and communication of life sciences research is vital to a robust scientific enterprise
- Promoting a culture of responsibility relies on education of the scientific community about dual use potential of life sciences research
- Institutions and investigators are best positioned to promote and strengthen responsible conduct and communication of results
- Effective oversight helps build and maintain public trust in the life sciences research enterprise

U.S. Government DURC Policies and the Research Continuum



Gain-of-Function Research

Gain-of-Function (GOF)

- Gain-of-function is a term used to refer to any modification of a biological agent that confers new or enhanced activity
- Debate around subset of GOF studies that involve the generation of pathogens with pandemic potential
  - Studies that generate certain pathogens with enhanced pathogenicity or transmissibility (by respiratory droplets) in mammals
  - GOF studies that have raised concerns are often cited as examples of DURC
  - Debate about risks and benefits

Potential Benefits and Risks- GOF Studies

- **Potential Benefits**
  - Help define the fundamental nature of human-pathogen interactions
  - Enable assessment of the pandemic potential of emerging infectious agents
  - Inform public health and preparedness efforts
  - Further medical countermeasure development

- **Potential Risks**
  - May involve generating engineered pathogens that could pose a pandemic threat if they were to be accidentally or intentionally released
  - May generate information that could be misused to threaten public health or national security
  - Risks would increase as more labs perform this type of research

GOF Studies Raise Questions

Los Angeles Times

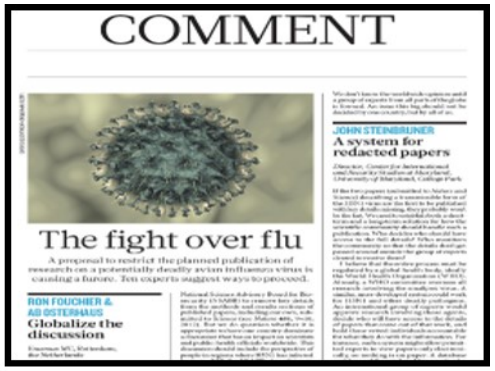
Fear Gone Viral

Despite government alarm bells, recent research with ferrets didn't create flu strains that threaten the world… there's really not much cause for alarm

The Independent

Alarm as Dutch lab creates highly contagious killer flu

Some scientists are questioning whether the research should ever have been undertaken in a university laboratory, instead of at a military facility.



The New York Times

An Engineered Doomsday

…the research should never have been undertaken because the potential harm is so catastrophic

nature

Don't censor life-saving science

Controlling who is allowed access to information about mutations in the H5N1 bird flu virus is unacceptable

- **Results of two NIH-funded studies on respiratory transmission of HPAI H5N1 raised biosecurity concerns**
- **A debate over whether and how the information contained in the manuscripts should/could be shared ensued with calls ranging from publishing in full to redaction and classification of the research**

The GOF Debate

For any experiment, the expected net benefits should outweigh the risks. Experiments involving the creation of potential pandemic pathogens should be curtailed until there has been a quantitative, objective and credible assessment of the risks, potential benefits, and opportunities for risk mitigation, as well as comparison against safer experimental approaches.

– Cambridge Working Group

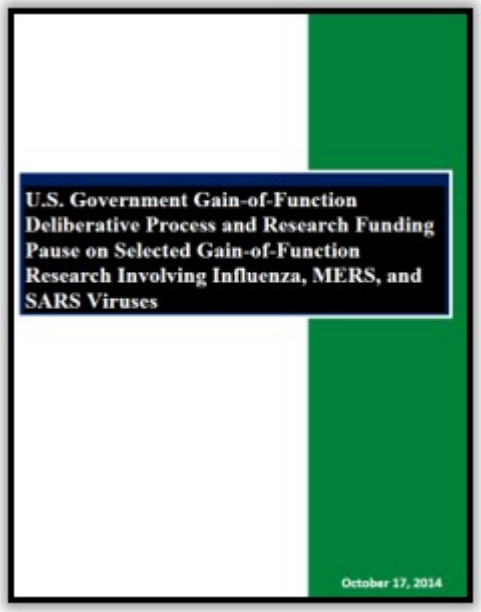
If we expect to continue to improve our understanding of how microorganisms cause disease we cannot avoid working with potentially dangerous pathogens. In recognition of this need, significant resources have been invested globally to build and operate BSL-3 and BSL-4 facilities, and to mitigate risk in a variety of ways, involving regulatory requirements, facility engineering and training. Ensuring that these facilities operate safely and are staffed effectively so that risk is minimized is our most important line of defense, as opposed to limiting the types of experiments that are done.

– Scientists for Science

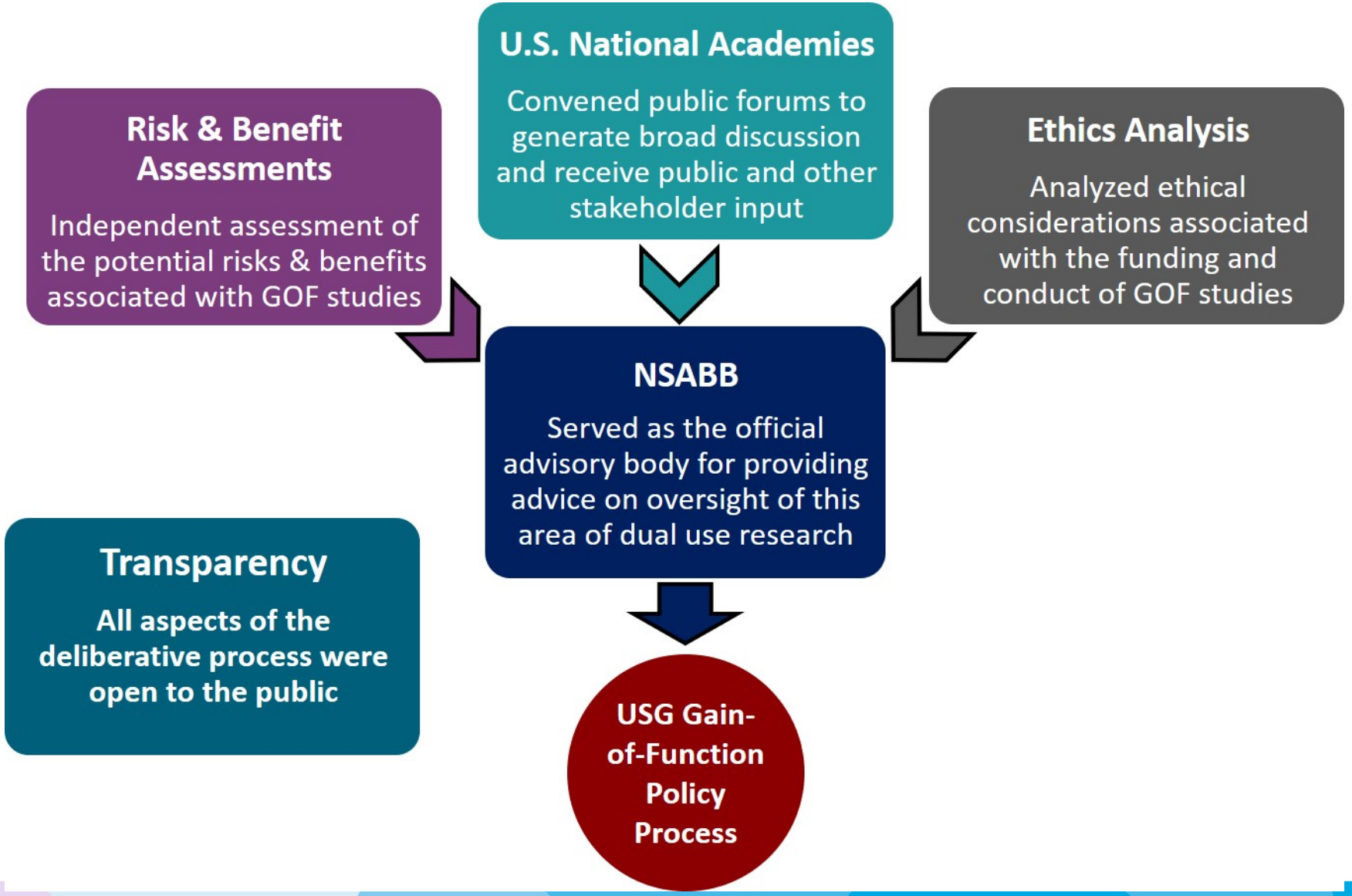
GOF Deliberative Process and Research Funding Pause

- **Deliberative Process**
  USG re-evaluated potential risks and benefits associated with GOF research involving pathogens with pandemic potential

- **Research Funding Pause**
  Accompanied by a pause in funding for projects that may be reasonably anticipated to generate influenza, MERS, or SARS viruses with enhanced pathogenicity and/or transmissibility in mammals via respiratory route



GOF Deliberative Process



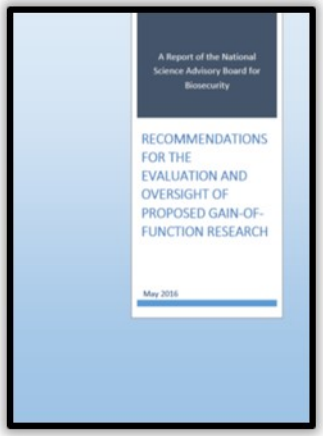
GOF Deliberative Process: Stakeholder Input

- **The deliberative process was designed to facilitate robust stakeholder input and included:**
  - **8 public meetings (6 NSABB; 2 National Academies)**
  - **~100 invited speakers, presenters, and panelists**
  - **~50 experts interviewed for the risk/benefit assessment**
  - **~50 public commenters (written and oral)**

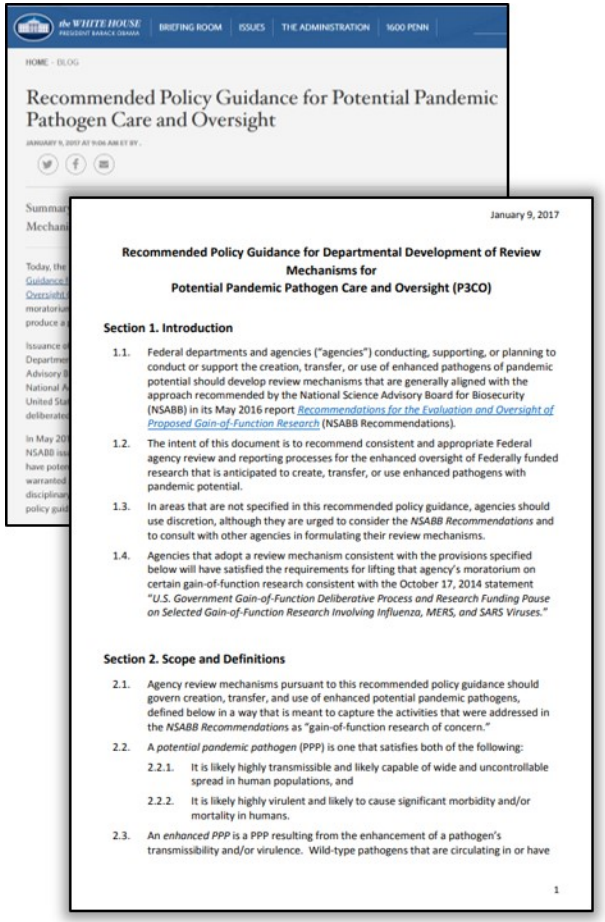
NSABB Role- GOF Deliberative Process

- **NSABB developed recommendations for the evaluation and oversight of gain-of-function research involving pathogens with pandemic potential**

- **NSABB Report (May 2016)**
  - **Central finding: Studies anticipated to enhance pathogens with pandemic potential have potential public health benefits but also entail significant potential risks**
  - **Recommended additional, multidisciplinary Department-level evaluation prior to funding decision, and appropriate ongoing oversight if funded**



U.S. Government Policies for PPP Care and Oversight (P3CO)



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Recommended Policy Guidance for Potential Pandemic Pathogen Care and Oversight

January 9, 2017

Recommended Policy Guidance for Departmental Development of Review Mechanisms for Potential Pandemic Pathogen Care and Oversight (P3CO)

Section 1. Introduction

1.1. Federal departments and agencies ("agencies") conducting, supporting, or planning to conduct or support the creation, transfer, or use of enhanced pathogens of pandemic potential should develop review mechanisms that are generally aligned with the approach recommended by the National Science Advisory Board for Biosecurity (NSABB) in its May 2016 report *Recommendations for the Evaluation and Oversight of Proposed Gain-of-Function Research* (NSABB Recommendations).

1.2. The intent of this document is to recommend consistent and appropriate Federal agency review and reporting processes for the enhanced oversight of Federally funded research that is anticipated to create, transfer, or use enhanced pathogens with pandemic potential.

1.3. In areas that are not specified in this recommended policy guidance, agencies should use discretion, although they are urged to consider the *NSABB Recommendations* and to consult with other agencies in formulating their review mechanisms.

1.4. Agencies that adopt a review mechanism consistent with the provisions specified below will have satisfied the requirements for lifting that agency's moratorium on certain gain-of-function research consistent with the October 17, 2014 statement *"U.S. Government Gain-of-Function Deliberative Process and Research Funding Pause on Selected Gain-of-Function Research Involving Influenza, MERS, and SARS Viruses."*

Section 2. Scope and Definitions

2.1. Agency review mechanisms pursuant to this recommended policy guidance should govern creation, transfer, and use of enhanced potential pandemic pathogens, defined below in a way that is meant to capture the activities that were addressed in the *NSABB Recommendations* as "gain-of-function research of concern."

2.2. A *potential pandemic pathogen* (PPP) is one that satisfies both of the following:

2.2.1. It is likely highly transmissible and likely capable of wide and uncontrollable spread in human populations, and

2.2.2. It is likely highly virulent and likely to cause significant morbidity and/or mortality in humans.

2.3. An *enhanced PPP* is a PPP resulting from the enhancement of a pathogen's transmissibility and/or virulence. Wild-type pathogens that are circulating in or have

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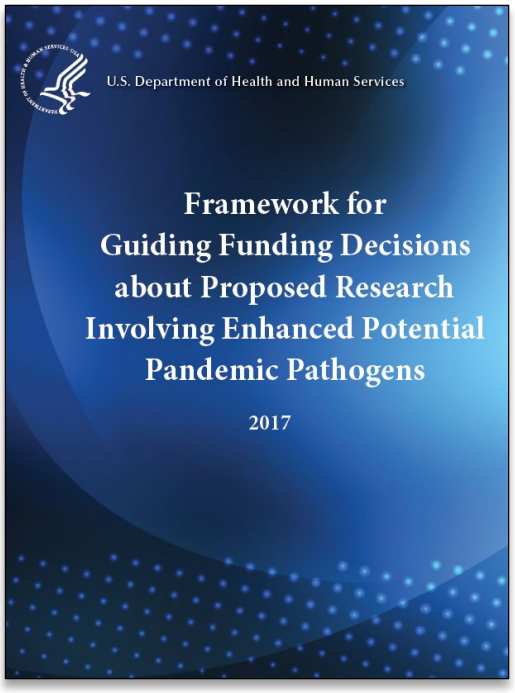
- **Jan 2017: *OSTP Recommended Policy Guidance for Departmental Development of Review Mechanisms for PPP Care and Oversight* directs federal departments and agencies considering funding projects anticipated to involve the creation, transfer, or use of enhanced PPP to adopt a department-level, multidisciplinary, pre-funding review mechanism.**
- **A "*potential pandemic pathogen*" (PPP) is one that is both**
  - **Likely highly transmissible and likely capable of wide and uncontrollable spread in human populations**
  - **Likely highly virulent and likely to cause significant morbidity and/or mortality in humans**
- **An *enhanced PPP* is a PPP resulting from enhancement of a pathogen's transmissibility or virulence.**

U.S. Government Policies for PPP Care and Oversight

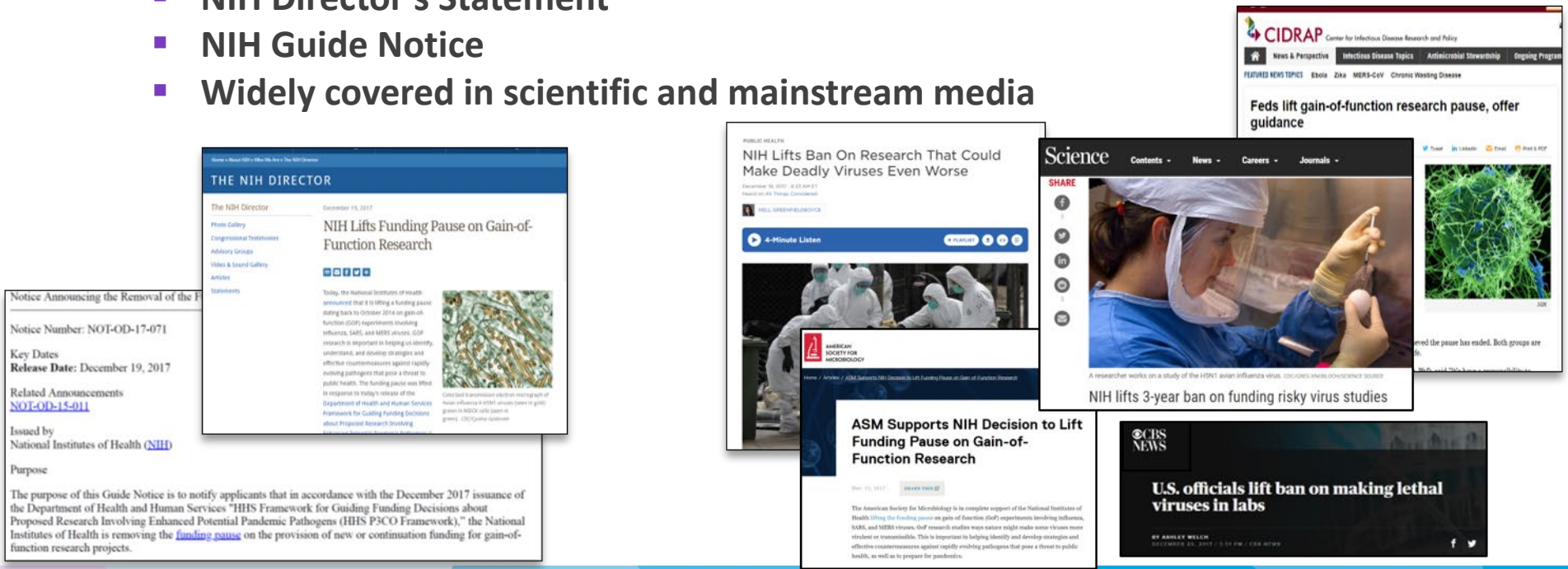


Dec 2017: *HHS Framework for Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens (HHS P3CO Framework)*

- **Ensures a multidisciplinary, Department-level pre-funding review and evaluation of proposed research meeting the scope outlined**
- **Intended to guide HHS funding decisions on individual proposed research that is reasonably anticipated to create, transfer, or use enhanced PPPs**
- **Seeks to preserve the benefits of life sciences research involving enhanced PPPs while minimizing potential biosafety and biosecurity risks**

HHS Lifts GOF Funding Pause

- **In Dec 2017, HHS publicly announced adoption of *HHS P3CO Framework* which allowed HHS to begin considering relevant research proposals under the new review mechanism**
  - **HHS Science, Safety, and Security (S3) website (also includes NIH Reporter links for funded projects reviewed under the HHS Framework)**
  - **NIH Director's Statement**
  - **NIH Guide Notice**
  - **Widely covered in scientific and mainstream media**



Additional Information & Resources

- Science, Safety, Security (S3)
  - http://www.phe.gov/s3/Pages/default.aspx

- NIH Office of Science Policy
  - Website: http://osp.od.nih.gov/
  - Blog: http://osp.od.nih.gov/under-the-poliscope
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