

NSABB Working Group Draft Report:

Recommendations for the Evaluation and Oversight of Proposed Gain-of-Function Research

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THE CHARGE TO THE NSABB

- 1. Advise on the design, development, and conduct of risk and benefit assessments for GOF studies**
 - Framework for Conducting Risk and Benefit Assessments of Gain-of-Function Research (May 2015)
- 2. Provide recommendations to the U.S. government on a conceptual approach to the evaluation of proposed GOF studies**
 - Draft Report: Recommendations for the Evaluation and Oversight of Proposed Gain-of-Function Research (May 2016)

NSABB DELIBERATIONS & CONSULTATIONS

- 1. Evaluation of potential risks and benefits of certain GOF research**
 - *Commissioned RBA of GOF studies (Gryphon Scientific)*
- 2. Ethical issues and decision-making strategies**
 - *Commissioned Ethical Analysis (Prof. Michael Selgelid)*
- 3. Domestic and international policies and guidelines and potential policy options**
 - *Briefings from subject matter experts; examination of literature; USG documents*
- 4. Stakeholder perspectives**
 - *NSABB and WG meetings*
 - *National Academies meetings on GOF research*
 - *Public comments*

ADVISING ON THE RISK AND BENEFIT ASSESSMENTS (RBA)

NSABB approved its Framework to guide the RBA in May 2015. The Framework recommended a number of features and principles to guide the development and conduct of the RBA:

1. Pathogens and pathogen characteristics that should be analyzed in the RBA
2. Categories of risks and benefits that should be assessed
3. Types of scenarios and events that should be evaluated in the RA
4. Methodologies for evaluating risks and benefits

FRAMEWORK FOR CONDUCTING RISK
AND BENEFIT ASSESSMENTS OF
GAIN-OF-FUNCTION RESEARCH

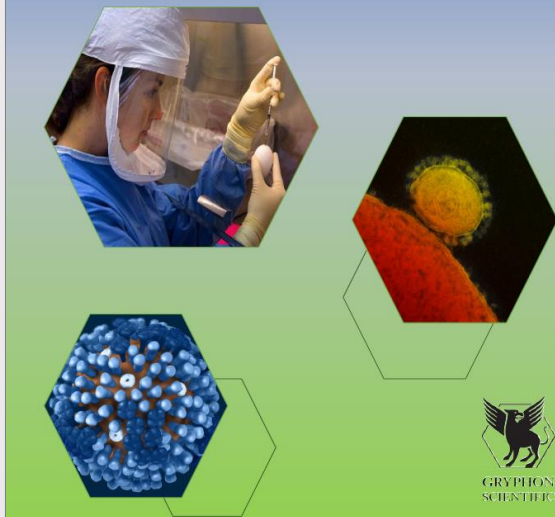
RECOMMENDATIONS OF THE NATIONAL SCIENCE ADVISORY
BOARD FOR BIOSECURITY

National Science Advisory Board for Biosecurity
MAY 2015

RISK AND BENEFIT ASSESSMENTS

Risk and Benefit Analysis of Gain of Function Research

Final Report—April 2016



<http://www.gryphonscientific.com/gain-of-function/>

- **Biosafety risk assessment** – risks associated with potential laboratory accidents involving GOF studies and pathogens with different enhanced phenotypes
- **Biosecurity risk assessment** – malevolent threats as they might pertain to laboratories involving GOF research or pathogens with enhanced phenotypes
 - **Information risk assessment** – risks resulting from the misuse of information that might be generated by certain GOF studies
- **Benefits assessment** – potential benefits of GOF studies, including potential unique benefits as well as alternative approaches that may achieve the same or similar benefits

RISK AND BENEFIT ASSESSMENTS

The RBA allowed the NSABB to:

- Understand the different risks associated with research involving certain pathogens and certain GOF experiments
- Identify and distinguish GOF studies that raise significant concerns from those that do not
- Identify and evaluate the potential benefits of GOF studies
- Consider the potential benefits derived from GOF studies compared to those that may be achieved through alternative approaches

ETHICAL ANALYSIS

 MONASH University
Centre for Human Bioethics

WHITE—PAPER

GAIN-OF-FUNCTION RESEARCH:
ETHICAL ANALYSIS

Professor Michael J. Selgelid
Director, Centre for Human Bioethics
Monash University, Melbourne, Australia

- Review and summary of ethical literature on GOF research
- Identification and analysis of existing ethical and decision-making frameworks applicable to GOF research
- A proposed ethical and decision-making framework for consideration by the NSABB

<http://osp.od.nih.gov/office-biotechnology-activities/biosecurity/nsabb>

ETHICAL ANALYSIS

Important values to consider when evaluating research proposals involving GOF studies and establishing mechanisms to review and/or make funding decisions:

Substantive Values

- Non-maleficence
- Beneficence
- Social justice
- Respect for persons
- Scientific freedom
- Responsible stewardship

Procedural Values

- Public participation & democratic deliberation
- Accountability
- Transparency

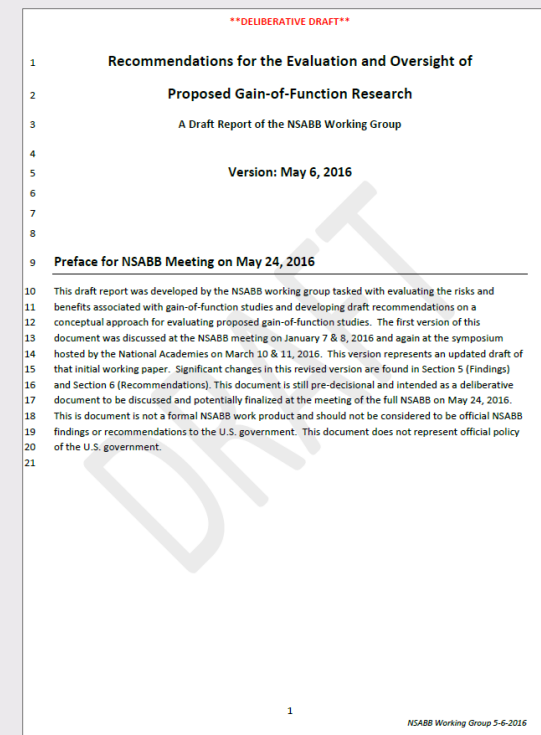
CURRENT FEDERAL POLICY LANDSCAPE

- **Scientific Merit Review**
- **Biosafety Oversight**
 - *Biosafety in Microbiological and Biomedical Laboratories (BMBL)*
 - *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)*
- **HHS Framework for guiding funding decisions about certain GOF studies**
- **Federal Select Agent Program**
- **Federal and Institutional Oversight of Life Science Dual Use Research of Concern**

A CONCEPTUAL APPROACH TO EVALUATING PROPOSED GOF STUDIES

Draft Report details the NSABB WG's:

- **Deliberative Approach**
 - Guiding principles for NSABB deliberations
- **Analyses**
 - Analysis and interpretation of the RBA
 - Consideration of ethical values
 - Decision-making strategies and frameworks for evaluating risks and developing policy
 - Examination of the current policy landscape
- **Findings**
- **Draft Recommendations**



<http://osp.od.nih.gov/office-biotechnology-activities/biosecurity/nsabb>

A CONCEPTUAL APPROACH TO EVALUATING PROPOSED GOF STUDIES

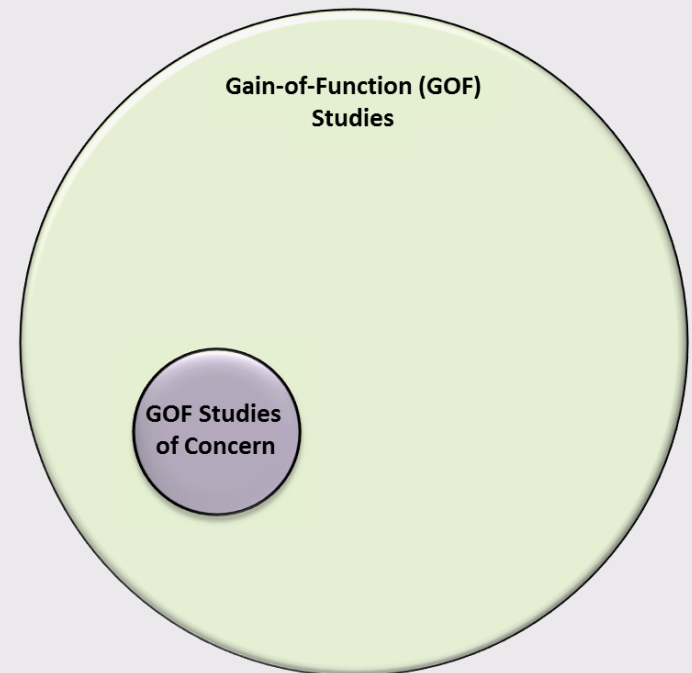
Revision of Dec. 2015 Draft Working Paper was based on:

- Substantial discussion and feedback
 - NSABB meeting (Jan. 2016)
 - 2nd NAS Symposium on GOF (Mar. 2016)
- Additional briefings and WG deliberation
- Public comments from various stakeholders

FINDINGS OF THE NSABB WG

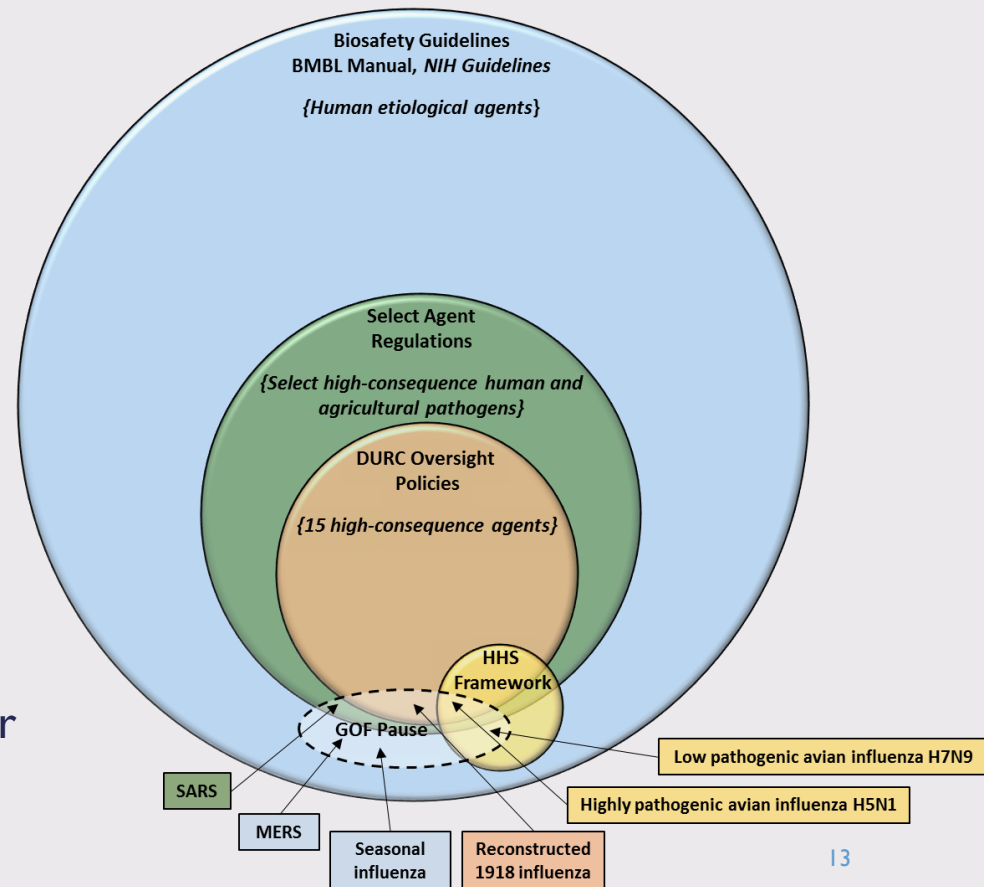
- **Finding I.** There are many types of GOF studies and not all of them have the same level of risks. Only a small subset of GOF--**GOF research of concern (GOFROC)**--research entail risks that are potentially significant enough to warrant additional oversight.

GOFROC is research that has the potential to **generate pathogens with pandemic potential** in humans by exhibiting high transmissibility and high virulence.



FINDINGS OF THE NSABB WG

- **Finding 2.** The U.S. government has several policies in place for identifying and managing risks associated with life sciences research. There are several points throughout the research life cycle where, if the policies are implemented effectively, risks can be managed and oversight of GOF research of concern could be implemented.
- **Finding 3.** Oversight policies vary in scope and applicability, and do not cover all potential GOFROC, therefore, **current oversight is not sufficient for all GOF research of concern.**



FINDINGS OF THE NSABB WG

- **Finding 4. An adaptive policy approach** is a desirable way to ensure that oversight and risk mitigation measures remain commensurate with the risks associated with the research and the benefits of the research are being fully realized.
- **Finding 5.** There are life sciences research studies, including possibly some GOF research of concern, **that should not be conducted because the potential risks associated with the study are not justified by the potential benefits.** Decisions about whether specific GOFROC should be permitted will entail an **assessment of the potential risks and anticipated benefits associated with the individual experiment in question.** The scientific merit of a study is a central consideration during the review of proposed studies but other considerations, including legal, ethical, public health, and societal values are also important and need to be taken into account.

FINDINGS OF THE NSABB WG

- **Finding 6.** Managing risks associated with GOF research of concern, like all life sciences research, requires both **Federal-level and institutional oversight, awareness and compliance, and a commitment by all stakeholders to safety and security.**
- **Finding 7.** Funding and conducting GOF research of concern involves many issues that are **international in nature.**

NSABB DRAFT RECOMMENDATIONS

Recommendation 1. Research proposals involving GOF research of concern entail significant potential risks and should receive an additional, multidisciplinary review, prior to determining whether they are acceptable for funding. If funded, such projects should be subject to ongoing oversight at the Federal and institutional levels.

The NSABB working group has proposed a conceptual approach the evaluation and oversight of proposed GOFROC that involves:

1. Identifying GOFROC (2 attributes)
2. Guiding funding decisions for GOFROC (8 principles)
3. Process for GOFROC review and ongoing Federal and institutional oversight

IDENTIFYING GOFROC

GOF research of concern is research that can be reasonably anticipated to generate a pathogen with both of the following attributes:

1. The pathogen generated is likely highly transmissible and likely capable of wide and uncontrollable spread in human populations.

AND

2. The pathogen generated is likely highly virulent and likely to cause significant morbidity and/or mortality in humans.

GUIDING FUNDING DECISIONS FOR GOFROC PROPOSALS

Principles that should guide the review of and funding decisions about research proposals anticipated to involve GOF studies of concern:

- i. The research proposal has been evaluated by a peer-review process and determined to be scientifically meritorious, with high impact on the research field(s) involved.
- ii. The pathogen that is anticipated to be generated must be judged, based on scientific evidence, to be able to arise by natural processes.
- iii. An assessment of the overall potential risks and benefits associated with the project determines that the potential risks as compared to the potential benefits to society are justified.

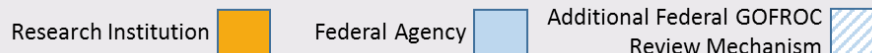
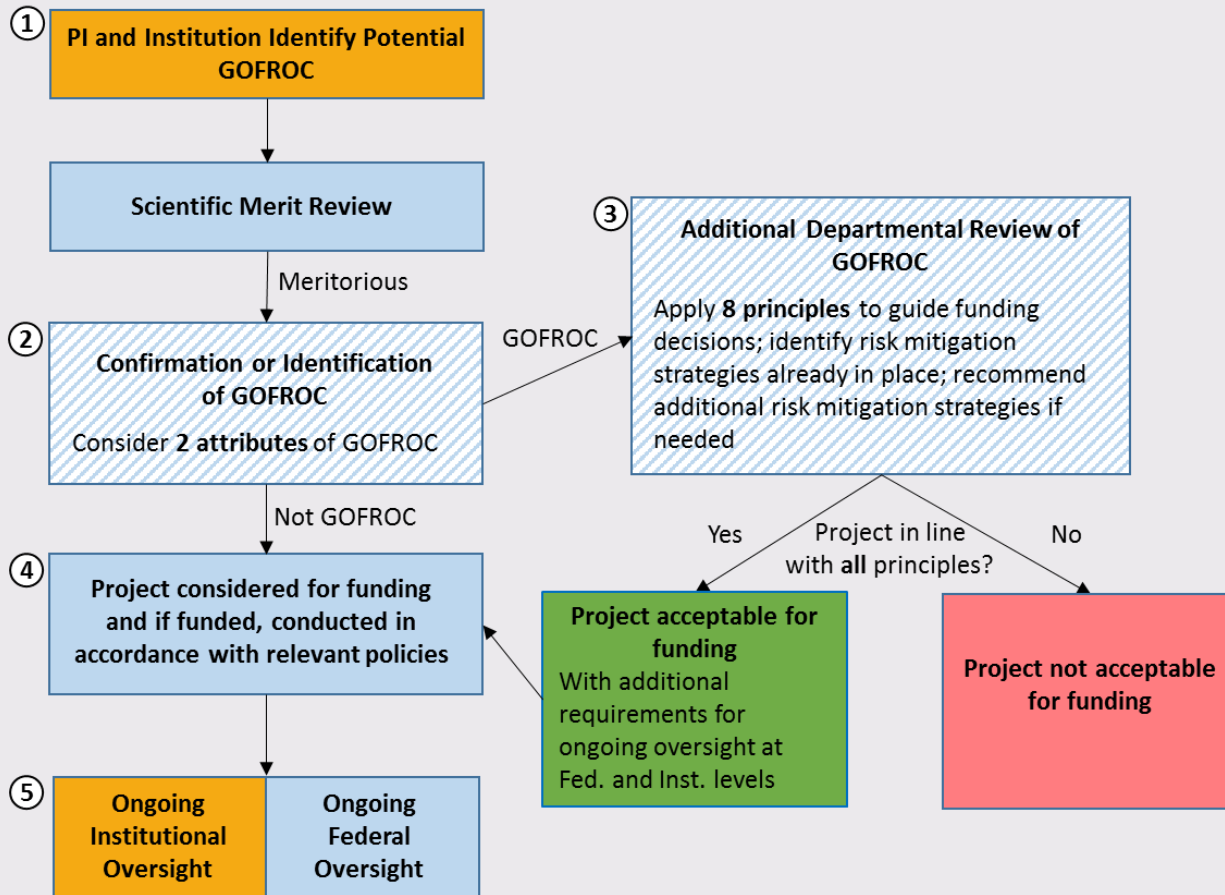
GUIDING FUNDING DECISIONS FOR GOFROC PROPOSALS

- iv. There are no feasible, equally efficacious alternative methods to address the same scientific question in a manner that poses less risk than does the proposed approach.
- v. The investigator and institution proposing the research have the demonstrated capacity and commitment to conduct it safely and securely, and have the ability to respond rapidly and adequately to laboratory accidents and security breaches.
- vi. The results of the research are anticipated to be broadly shared in compliance with applicable laws and regulations in order to realize its potential benefits to global health.

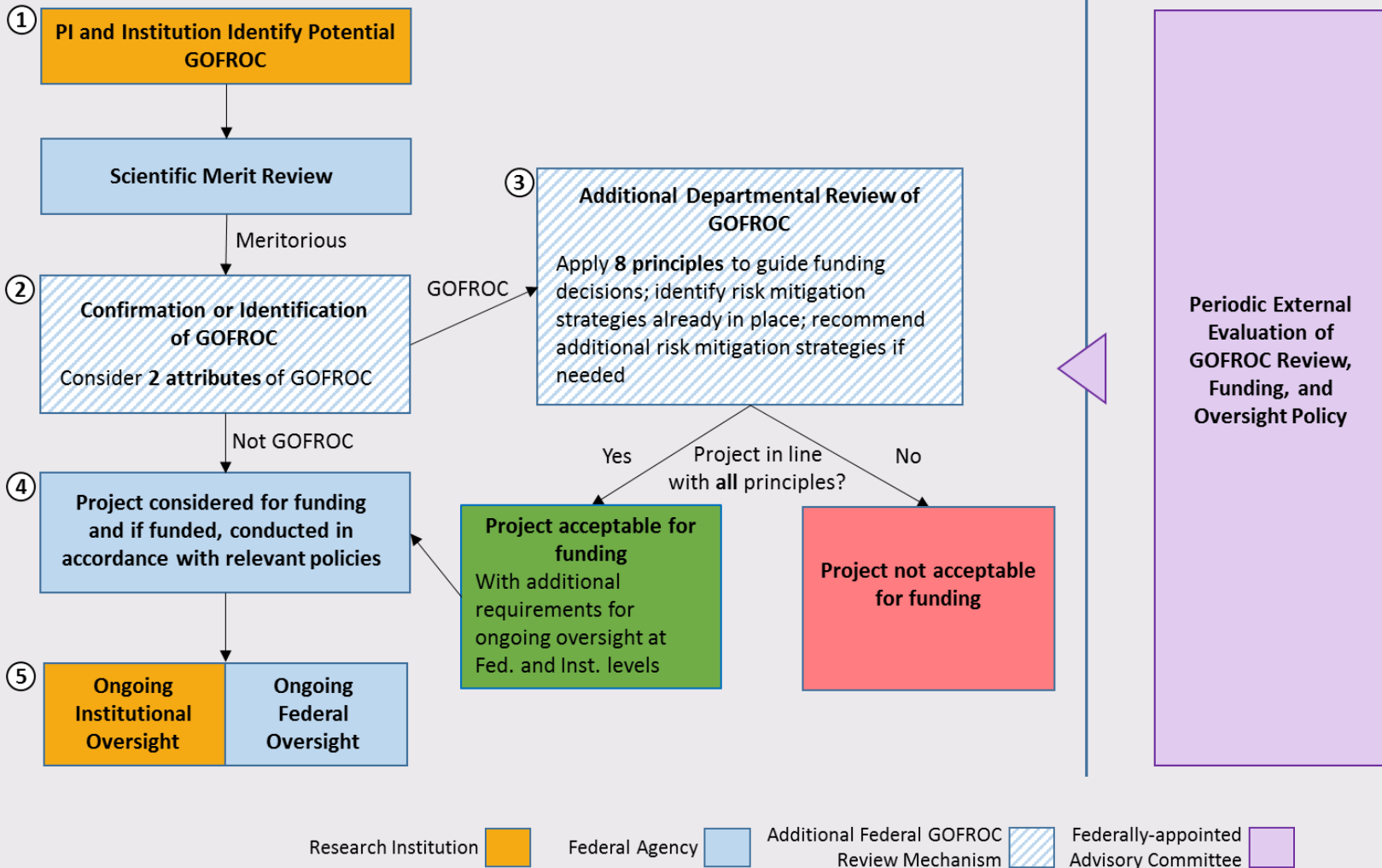
GUIDING FUNDING DECISIONS FOR GOFROC PROPOSALS

- vii. The research will be supported through funding mechanisms that allow for appropriate management of risks and ongoing Federal and institutional oversight of all aspects of the research throughout the course of the project.
- viii. The proposed research is ethically justifiable.

Proposed Process: Review, Funding, & Oversight for Research Proposals Involving GOFROC



Periodic Evaluation of Oversight Process for GOFROC



NSABB DRAFT RECOMMENDATIONS

Recommendation 2. An external advisory body that is designed for transparency and public engagement should be utilized as part of the U.S. government's ongoing evaluation of oversight policies for GOF research of concern.

Goals:

- Provide independent examination of policies for reviewing, funding, and conducting GOFROC
- Understand how decisions were made
- Identify challenges to implementing the policy
- Provide recommendations, as needed
- Provide transparency and promote public engagement
- Facilitate continued dialogue about GOFROC

NSABB DRAFT RECOMMENDATIONS

- **Recommendation 3.** The U.S. government should pursue an **adaptive policy approach** to help ensure that oversight remains commensurate with the risks associated with the GOF research of concern.
 - **Recommendation 3.I.** The U.S. government should consider developing a system to **collect and analyze data about laboratory safety incidents** to inform GOF research of concern policy development over time.
- **Recommendation 4.** In general, oversight mechanisms for GOF research of concern should be **incorporated into existing policy frameworks when possible.**
- **Recommendation 5.** The U.S. government should consider ways to ensure that all GOF research of concern conducted within the U.S. or by U.S. companies **be subject to oversight, regardless of funding source.**

NSABB DRAFT RECOMMENDATIONS

- **Recommendation 6.** The U.S. government should undertake broad efforts to strengthen laboratory biosafety and biosecurity and, as part of these efforts, seek to **raise awareness about the specific issues associated with GOF research of concern.**
- **Recommendation 7.** The U.S. government should **engage the international community** in a dialogue about the oversight and responsible conduct of GOF research of concern.



QUESTIONS?