Session II
Examination of Ethical Issues Associated with Gain-of-Function Studies and Discussion of Potential Decision Frameworks

Moderators:
Susan M. Wolf, J.D.
Francis L. Macrina, Ph.D.
Members, NSABB Working Group

Examination of Ethical Issues Associated with Gain-of-Function Studies

Purpose

The RBA provides information about risks and benefits associated with GOF studies but interpreting that information and making policy recommendations requires judgements and values

To aid the NSABB in its deliberations the USG commissioned an ethical analysis that:

- Reviews the ethical literature associated with GOF studies
- Discusses existing ethical and decision-making frameworks
- Proposes an ethical and decision-making framework for NSABB to consider when crafting its final recommendations

Examination of Ethical Issues – Values

NSABB WG has begun identifying values that should inform deliberations on GOF studies

- Substantive values that should be considered include:
  - Non-maleficence
  - Beneficence
  - Social justice
  - Respect for persons
  - Scientific freedom
  - Responsible stewardship
- Important procedural values in decision-making include:
  - Public participation and democratic deliberation
  - Accountability
  - Transparency

Decision-Making Strategies for Managing Risks

NSABB WG has considered a number of decision-making strategies, including the following. These, and others, are discussed in the WG's working paper and Professor Selgelid's paper.

- **Maximax –** choose the option with the best possible outcome
- **Expected Utility –** choose the option that maximizes expected utility, where expected utility for a possible outcome = probability x utility
- **Maximin –** choose the option with best outcome among the worst possible outcomes
- **Precaution –** take reasonable measures to prevent, minimize, or mitigate risks that are significant and plausible

Session II – Examination of Ethical Issues Associated with Gain-of-Function Studies and Discussion of Potential Decision Frameworks

White Paper

Gain-of-Function Research: Ethical Analysis

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

1. Introduction

Gain-of-function (GOF) research involves experimentation that aims, or is expected, to increase the transmissibility and/or virulence of pathogens. Such research (when conducted by responsible scientists) usually aims to improve understanding of disease causing agents, their interaction with human hosts, and/or their potential to cause pandemics. The ultimate objective of such research is to better inform public health and preparedness efforts and/or development of medical countermeasures. Despite these important potential benefits, GOF research (GOFR) can pose risks regarding biosecurity and biosafety.

GOFR is a subset of 'dual use research'—i.e., research that can be used for both beneficial and malevolent purposes (NRC 2004; Miller and Selgelid 2008). 'Dual use research of concern' (DURC) refers to dual use research for which the consequences of malevolent use would be exceptionally severe (whereas almost any research might be considered "dual use" broadly conceived—because almost any research, or just about anything for that matter, can be used for some malevolent purpose or other). Of particular concern in the context of life science research is that advances in biotechnology may enable development and use of a new generation of biological weapons of mass destruction.

DURC has thus been one of the most hotly debated science policy issues during the 21st century, with controversy surrounding a series of published experiments with potential implications for biological weapons making. Such studies include the genetic engineering of a mousepox virus in 2001 (Jackson et al. 2001), the artificial synthesis (via synthetic genomics) of a 'live' polio virus from chemical components in 2002 (Cello et al. 2002), and the reconstruction (via synthetic genomics) of the 1918 'Spanish Flu' virus in 2005 (Tumpey et al. 2005). Though all of these studies involved legitimate aims, critics argued that they should not have been conducted and/or published. Some argued that publishing studies like these in full detail provided "recipes" for especially dangerous potential biological weapons agents to would-be bioterrorists. Many who acknowledged such potential dangers, on the other hand, argued that benefits of publication outweighed risks involved.

The most controversial dual use life science experiments to date involved the creation of highly pathogenic H5N1 (avian) influenza virus strains that were airborne transmissible between ferrets, which provide the best model for influenza in humans (Herfst et al. 2012; Imai et al. 2012). This research aimed to answer an important scientific question—i.e., Might it be possible for H5N1 to naturally evolve into a human-to-human transmissible strain and thus result in a pandemic?—and (purportedly) yielded an affirmative answer. After the US National

Presenter:

Michael Selgelid, Ph.D.
Principal Author, commissioned Ethical Analysis of GOF Research

Discussion Panelists:

- **R. Alta Charo, J.D., University of Wisconsin Law School**
- **Jonathan Moreno, Ph.D., University of Pennsylvania**
- **David Fidler, J.D., M.Phil., Indiana University, Bloomington**
- **John Kadvany, Ph.D., Independent consultant on decision science**

Submit questions: nsabb@od.nih.gov

Examination of Ethical Issues – Discussion

<u>Questions for Discussion</u>

- What ethical values should NSABB consider in moving beyond the risk and benefit assessments in order to formulate policy recommendations on GOF studies involving pathogens with pandemic potential?
- What ethical or other decision-making frameworks should be brought to bear when considering whether to fund and conduct certain GOF studies?
- How can ethical decisions be made in light of the inherent uncertainty associated with potential risks and benefits?
- Is there GOF research that should not be funded or conducted? If so, what are the features of such studies and what considerations should guide the identification of GOF studies that might meet such designation?