Preliminary Draft Findings & Recommendations

This document is intended to provide a basis for discussion and consideration of preliminary draft findings and recommendations to help inform ongoing deliberations of the NSABB Working Group to Review and Evaluate Potential Pandemic Pathogen Care and Oversight (P3CO) Policy.

Policy scope and definitions

Finding 1. Potential pandemic pathogen (PPP) and enhanced PPP (ePPP) definitions. The definitions of PPP and ePPP fail to adequately encompass pathogens that do not meet the threshold of "likely highly virulent", but which could also pose a severe threat to public health or national security if the pathogen was capable of wide and uncontrollable spread in human populations.

Recommendation 1. The definitions of PPP and ePPP should be modified to reflect the fact that whether or not a pathogen poses a severe threat to public health, the capacity of health systems to function, or national security is a function of both transmissibility and virulence. Therefore, the definitions of PPP and ePPP should be modified to include potentially highly transmissible pathogens having low or moderate virulence or case-fatality rates as well as pathogens that are less transmissible but that have higher virulence or case-fatality rates. Examples should be provided as an element of policy implementation guidance to illustrate how modifications to a pathogen would or would not cross the threshold necessary to constitute an ePPP (see recommendation 4).

Finding 2. Exclusions and urgent review during public health emergencies. The identification of ePPP research is informed by the current body of scientific evidence, knowledge, and adequacy of biosafety controls, and necessarily entails some degree of uncertainty. It is therefore important for assessments and evaluations to be made in light of current scientific knowledge and to be updated in response to new findings. The focus for assessment should be on the potential for an activity or a modification to produce a pathogen that meets the criteria for an ePPP and not on the context in which this activity or modification is carried out.

All research activity that is reasonably anticipated to involve the creation, transfer, or use of ePPPs should be subject to the additional consideration under the U.S. Government (USG) P3CO framework. However, the often-critical contributions that surveillance and vaccine research activities make to public health response are recognized and necessitate mechanisms to ensure that if ePPP research is identified and deemed critical to public health or national security, its review should not be unduly delayed.

Recommendation 2. Because the review and evaluation of ePPP research considers risks and benefits, including whether the research is critical to public health or national security, the USG should reconsider the current exclusions for research activities associated with surveillance and vaccine development or production, which could be broadly interpreted as blanket exclusions. Processes should be instituted for urgent review or evaluation of ePPP research that is determined to be critical for a public health response or national security under a declared public health emergency, or as otherwise directed by the Secretary, Department of Health and Human Services.

Policy and implementation

Finding 3. Enhanced institutional responsibility. Investigators and institutions are critical components of a comprehensive oversight system, as they are most familiar with the research proposed to be or being conducted in their facilities and are in the best positions to promote and strengthen responsible conduct and ensure ongoing biosafety and biosecurity controls. The current P3CO policy does not adequately incorporate the local review and oversight roles played by investigators and institutions in the development, review, and ongoing oversight of research.

Recommendation 3.

- USG P3CO framework should articulate the specific roles, responsibilities, and expectations for investigators and institutions in the review or evaluation of research for potential involvement of ePPPs, taking into account existing review and oversight processes.
- Local compliance procedures should be better harmonized, strengthened where needed, and resourced.
- A USG contact entity should be designated to assist investigators and institutions in the review process and to provide oversight to ensure adequate evaluation.

Finding 4. P3CO policy and implementation directives. The additional review process outlined under the OSTP Recommended Policy Guidance for Departmental Development Mechanisms for Potential Pandemic Pathogen Care and Oversight (OSTP P3CO Policy Guidance) and HHS Framework for Guiding Funding Decisions of Proposed Research Involving Enhanced Potential Pandemic Pathogens (HHS P3CO Framework) are generally appropriate as designed at the federal department level. However, Section III.3 and III.4 of the OSTP P3CO Policy Guidance regarding risks and benefits are inconsistent with similar policies as described in the Belmont Report. Additionally, Section IV.C of the HHS P3CO Framework indicates extra care in reviewing proposed research that is reasonably anticipated to generate an outcome from one of the

seven categories of research outlined in that section is only required at the HHS department level review.

Beyond the HHS P3CO Framework, an implementation directive from HHS to HHS funding agencies is lacking. Guidance from the federal funding agency for research institutions and principal investigators are also lacking. Both are needed to effectively implement the HHS P3CO Framework. The lack of an implementation directive and guidance has contributed to uncertainty, resulting in a lack of clarity regarding the timing and expected requirements of the review process, and potential opportunity costs associated with investigators being deterred from pursuing important research or careers specializing in certain pathogens. Additional education and guidance would facilitate consistent and efficient implementation by all stakeholders and enhance awareness and consideration of potential biosafety and biosecurity issues throughout the research life cycle, including during the development of research proposals.

Recommendation 4. P3CO framework. Section III.3 and III.4 of the OSTP P3CO Policy Guidance should be modified to be consistent with the Belmont Report. For example, Section III.3 should be modified to, "There are no feasible, scientifically sound alternative ways of obtaining the benefits sought in the research in a matter that poses less risk". Section III.4, "Risks that are not necessary to answer an important scientific question have been eliminated and an overall assessment of remaining risks finds that they are justified by the potential benefits to society from the research."

The types of research of concern outlined in Section IV.C of the HHS P3CO Framework should be given extra care and considered throughout the research proposal and review process, by principal investigators, institutions, and federal funding agencies (including those outside HHS) in addition to the federal department-level review.

Implementation directives. The USG should dedicate resources and personnel to the development of an implementation directive/plan, additional guidance, educational materials, and standard operating procedures, including regarding ongoing oversight, that can be used or adapted by funding institutions, research institutions, and investigators when implementing the policy. The companion guide and other material developed to aid implementation of the USG dual use research of concern (DURC) policies may serve as a model. An implementation plan should outline clear roles and responsibilities for investigators, institutions, federal funding agencies, and federal departments. Guidance and education material should include:

- Steps, considerations, and criteria for identifying research that could generate ePPPs
- Types of questions and information considered at each stage of review
- Types of risks and benefits assessed (risks should include consideration of short and long-term risks and potential consequences)
- The expected components of material evaluated (e.g., risk/benefit analysis, risk mitigation plan, etc.)

- Substantive information on biosafety and biosecurity standards, controls, and safeguards
- Standards for review timelines under emergency and non-emergency conditions
- Expectations and standards for responsible communication of research

Other points to consider:

The USG should develop principles and guidelines that can be applied to substantiate, 1) there are no feasible, scientifically sound alternative methods of obtaining the benefits sought in the research in a manner that poses less risk; and 2) unnecessary risks have been eliminated and an overall assessment of remaining risks finds that they are justified by the potential benefits to society from the research.

Transparency and accountability

Finding 5. Review process transparency. Under the HHS P3CO Framework, proposed research identified by the funding agency as reasonably anticipated to create, transfer, or use ePPPs undergoes an additional multidisciplinary review by a federal department level review group. The review group constituted by HHS appears to have the appropriate expertise, and the process takes into account the need to protect potentially sensitive personal and proprietary information and facilitates open discussion of issues relevant to national security and public health preparedness within the review group. However, increased transparency in the review process is needed. This would enable a greater understanding of, and engender trust in, review and oversight processes for ePPP research.

Recommendation 5. The USG should take additional steps to increase transparency in the review process. This would in part be accomplished by development and release of an implementation plan and guidance (see recommendation 4), but the USG should also consider sharing a summary of key determinants and decisions of USG review.

Additional Working Group considerations

Finding 6. Animal and plant pathogens. The focus of the current USG P3CO framework on pathogens that are likely to cause disease in humans is appropriate. However, certain research involving enhanced pathogens may pose significant threats to animal and plant health, which could cause severe secondary impacts on human health, in addition to impacts on food security, economic security, and national security. The USG may need to consider development of analogous policies and processes for additional review and oversight of relevant research involving enhanced pathogens likely to pose severe threats to human health, food security,

economic security, or national security by its impacts on animals or plants or to animal or plant products.

Finding 7. P3CO and DURC. ePPP research can be considered a subset of DURC. There are substantive overlaps between the intent, purpose, and entities involved in the implementation of policies for the oversight of ePPP research and DURC. Acknowledging that the review and evaluation of USG DURC policies is ongoing, this Working Group supports consideration of possible revisions that would incorporate ePPP research into the DURC oversight framework. However, it remains important that the principles identified above be included in a proposed consolidation of ePPP research safeguards with DURC safeguards and that review and oversight processes and risk mitigation measures be commensurate with the degree of risk posed.