



### Abstract

The U.S. Government supports research on pathogens that pose threats to public health and national security. As part of its mission to enhance the health and well-being of Americans, the Department of Health and Human Services (HHS) supports research on pathogens that have the potential to advance our understanding of pathogenesis and mechanisms of disease, inform the development of medical countermeasures, prevent and treat infections, and guide disease surveillance and public health preparedness activities. However, the specific subset of studies that have the potential to generate pathogens with pandemic potential have raised some concerns. On January 9, 2017, the White House Office of Science and Technology Policy issued policy guidance requiring funding agencies to have a pre-funding mechanism in place for the review of a small subset of experiments that could potentially produce an enhanced pathogen with pandemic potential (PPP). In response, HHS has developed a multi-level, multi-disciplinary department-level review process that includes a risk-benefit analysis and review of risk mitigation plans for the conduct of enhanced PPP research.

### Definitions

**A PPP is likely highly transmissible and likely capable of wide and uncontrollable spread in human populations; and, is likely highly virulent and likely to cause significant morbidity and/or mortality in humans.**

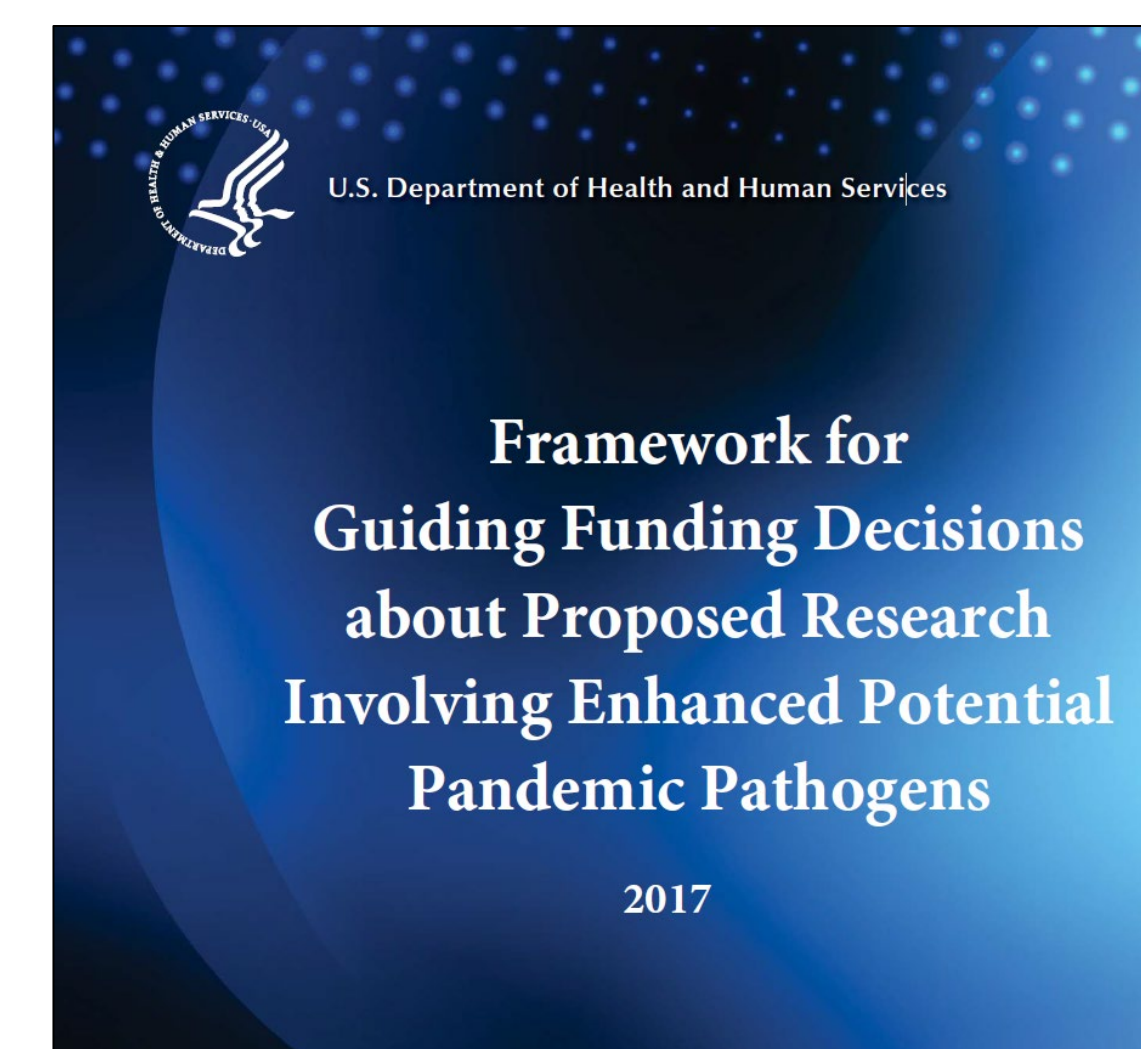
**An enhanced PPP is a PPP resulting from the enhancement of a pathogen's transmissibility and/or virulence.** The oversight system for enhanced PPP is complementary to that for biological select agents and toxins in that it is based on principles and practices for mitigating risk to public health and/or national security.

Wild-type pathogens that are circulating in, or have been recovered from, nature are not enhanced potential pandemic pathogens (PPPs), regardless of their pandemic potential. To the extent that transmissibility and/or virulence of PPPs are modified in the following categories of studies the resulting pathogens are not considered to be enhanced PPPs: Surveillance activities, including sampling and sequencing; and, Activities associated with developing and producing vaccines, such as the generation of high growth strains.

### Background

In 2013, a specific subset of studies, aimed at better understanding influenza in order to improve disease prevention and treatment, raised concerns about enhanced Potential Pandemic Pathogens (PPP). A major debate arose within the scientific community over the benefits of such research relative to the safety and security risks. In response, the U. S. Government imposed a funding pause in October 2014 on certain types of research on influenza, MERS, or SARS viruses.

The National Science Advisory Board for Biosecurity (NSABB) and the National Academies of Sciences, Engineering and Medicine (NASEM) initiated a deliberative process to determine how to balance the need for scientific discovery with the potential pandemic risks posed by the research. NASEM held two public workshops where there was general agreement on the need for greater oversight of a very small subset of research, referred to as enhanced potential pandemic pathogens (PPP) research. In May 2016, the NSABB's report, *Recommendations for the Evaluation and Oversight of Proposed Gain-of-Function Research*, concluded that a small subset of experiments could potentially create pathogens with enhanced pandemic potential. As a result, the NSABB recommended a multi-level, multi-disciplinary, and pre-funding review process that included a risk-benefit analysis of research on pathogens of pandemic potential and that detailed risk mitigation measures.

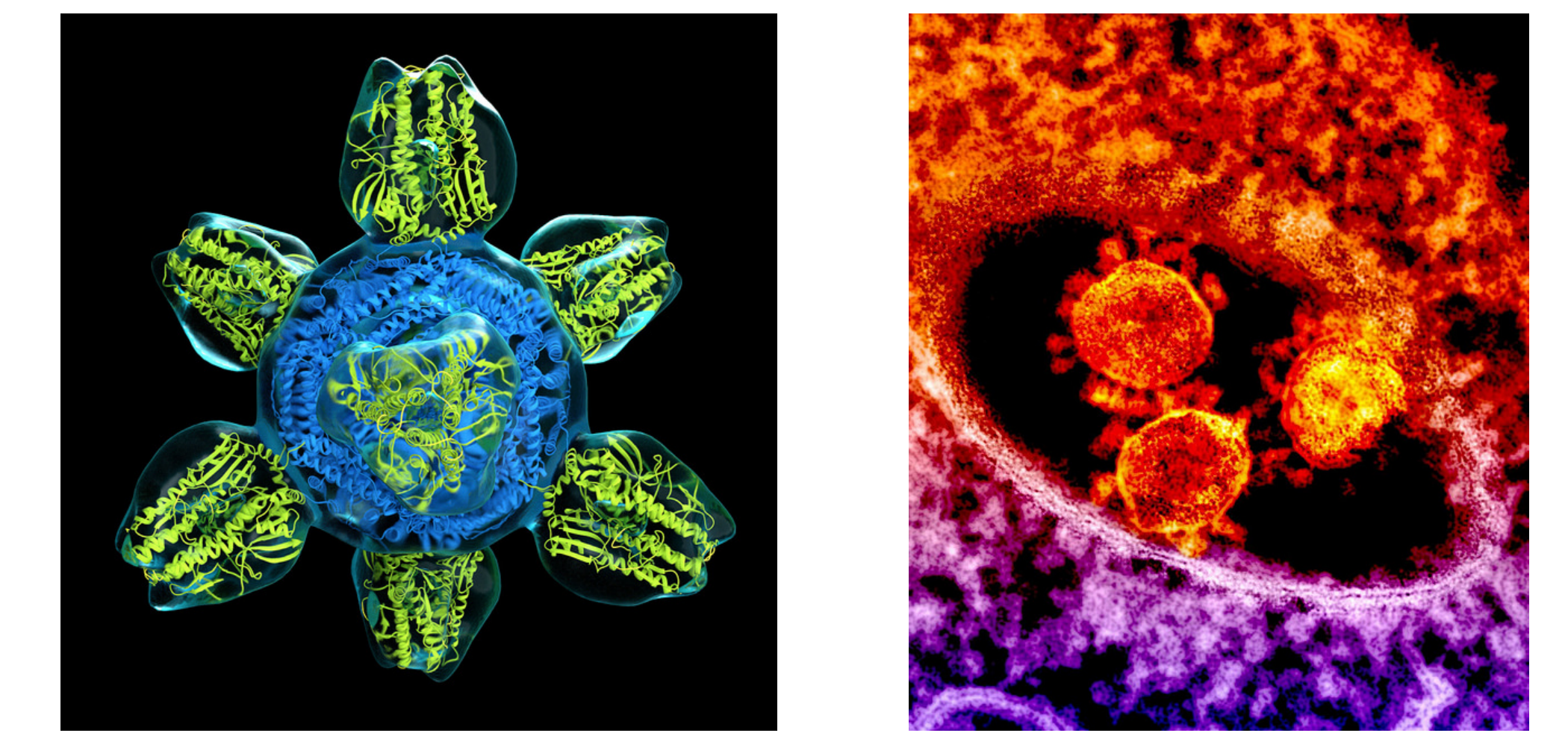


### Department of Health and Human Services Framework for Guiding Funding Decisions about Proposed Research involving Enhanced Potential Pandemic Pathogens

The HHS Framework Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens (*HHS P3CO Framework*) is intended to establish a prefunding process for the review of HHS proposed research that is reasonably anticipated to create, transfer, or use enhanced PPPs in order to guide funding decisions. The HHS P3CO Framework is approved - **lifting the pause on HHS funding of certain research that involves potential pandemic pathogens (PPP) and provides a method for department-level review.** HHS P3CO Framework supersedes the 2013 *HHS framework for guiding funding decisions about research proposals with the potential for generating highly pathogenic avian influenza H5N1 viruses that are transmissible among mammals by respiratory droplets.*

### HHS P3CO Review Criteria

1. Research is scientifically sound;
2. The pathogen is considered to be a credible source of a potential future human pandemic;
3. The potential risks as compared to the potential benefits to society are justified;
4. There is no feasible alternative method to address the same question in a manner that poses less risk;
5. The investigators have demonstrated the capacity and commitment to conduct the research safely and securely;
6. Research results are expected to be responsibly communicated;
7. The research will be subject to ongoing federal oversight; and
8. The research is ethically justifiable.



Representation of a universal flu vaccine and electron micrograph of MERS coronavirus particles. NIH image Gallery: <https://www.flickr.com/photos/nihgov/with/36461765782/>

### HHS P3CO Pre-Funding Review Process

The HHS P3CO Review is a two-step deliberative review process to guide funding decisions on proposed research that is reasonably anticipated to create, transfer, or use enhanced potential pandemic pathogens (PPP):

1. Funding agency review of research for scientific merit and criteria for enhanced PPP; and
2. Department-level multi-disciplinary review of research risks and benefits, ethical considerations and risk mitigation plans. Review expertise includes: Scientific research; Biosafety and biosecurity; Medical countermeasures - development and availability; Law; Ethics; Public health preparedness and response; Biodefense; Select agent regulations; Public health policy; Funding agency perspectives.

### Transparency and Public Engagement

Funding decisions will be communicated to the White House Office of Science Technology Policy and made available to the public; and,

HHS will periodically ask the NSABB to review the HHS P3CO Review Process.

### References

(<https://www.phe.gov/s3/dualuse/Pages/default.aspx>)

- 2017 Department of Health and Human Services' (HHS) *Framework for Guiding Funding Decisions About Proposed Research Involving Enhanced Potential Pandemic Pathogens* (HHS P3CO Framework)
- January 9, 2017, *Recommended Policy Guidance for Departmental Development of Review Mechanisms for Potential Pandemic Pathogen Care and Oversight* (P3CO)
- May 2016 National Science Advisory Board for Biosecurity (NSABB) report, *Recommendations for the Evaluation and Oversight of Proposed Gain-of-Function Research*
- October 17, 2014 *U.S. Government Gain-of-Function Deliberative Process and Research funding Pause on Selected Gain-of-Function Research Involving Influenza, MERS, and SARS Viruses.*