Compiled Public Comments on National Science Advisory Board for Biosecurity (NSABB) Meeting

September 14, 2022 –

November 3, 2022

Public Comments:

1 Richard H. Ebright, Rutgers University
2 Nariyoshi Shinomiya, National Defense Medical College (Japan)
3 Tom Inglesby, Anita Cicero, Jaspreet Pannu, Marc Lipsitch, David Relman
4 Mary Lee Watts, Stefano Bertuzzi, The American Society for Microbiology (ASM)

Submission Date: 9/14/22

Name: Richard H. Ebright

Name of Organization: Rutgers University

Comment:

Through this message, I am submitting written public comments for the September 21st NSABB Virtual Meeting,

Please see the attached PDF file with my written comments.

Additional Comment (attachment):

THE STATE UNIVERSITY OF NEW JERSEY
RUTGERS

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September 13, 2022

RE: Potential Pandemic Pathogen Care and Oversight (P3CO) Policy Review

Dear Colleagues:

I wish to submit the following public on the Potential Pandemic Pathogen Care and Oversight (P3CO) Framework:

> Lapses in oversight of enhanced potential pandemic pathogens research (ePPP research)) may have caused the current pandemic and could cause future pandemics. The US government funded high-risk gain-of-function research and enhanced potential pathogen research at the Wuhan Institute of Virology in 2016-2019. The research overlapped the Research Funding Pause on Selected Gain-of-Function Research Involving Influenza, MERS, and SARS Viruses that was in effect in the 2014 to 2016, and met the criteria to be paused, but was not paused. The research also overlapped the HHS Framework for Research Involving Enhanced Potential Pandemic Pathogens (P3CO Framework) that has been in effect since 2017, and met the criteria for federal risk-benefit review under the P3CO Framework, but did not undergo federal risk-benefit review under the P3CO Framework. The research was performed at biosafety level 2--a biosafety level that is patently inadequate for ePPP research. The research may have encountered or created SARS-CoV-2 or a proximal progenitor, and an accident in the research may have been responsible for entry of SARS-CoV-2 or a proximal progenitor into the human population.
>
> These facts--and these statements indeed are facts--are an indictment of the current system of oversight of ePPP research and are a testament that a new system of oversight of ePPP research is essential.
>
> Moving forward, any effective system of oversight of ePPP research must address seven serious defects of the current system:
>
> > (1) Currently, almost no ePPP research, not even the very-highest-risk ePPP research, undergoes the risk-benefit review mandated under the P3CO Framework, because federal funding agencies fail to forward most proposals for ePPP research to the P3CO Committee for review. In the six years since the P3CO Framework was implemented, only three ePPP-research projects underwent review by the P3CO Committee. Most ePPP-research projects-including the project in Wuhan--were not forwarded by to the P3CO Committee and did not undergo review by the P3CO Committee.

All ePPP research should undergo the risk-benefit review mandated under the P3CO Framework. All ePPP proposals automatically--without exceptions-should be forwarded to the P3CO Committee and should be reviewed by the P3CO Committee. For compliance with federal regulations on select-agent, human-subjects, and vertebrate-animals research, federal funding agencies employ checklists of agents and activities, in which a positive response automatically--without exceptions--triggers review. For ePPP research, an analogous checklist of agents and activities, should automatically-- without exceptions--trigger review.

(3) Currently, oversight of ePPP research covers only research institutions that receive federal funding. Research institutions not receiving federal funding--for example privately funded research institutions--are not covered.

Oversight of ePPP research should cover all institutions, irrespective of funding source.

(4) Currently, there are no regulations with force of law for oversight of ePPP research. Decisions of the P3CO Committee are not binding. and compliance is not mandated, monitored, or enforced.

Oversight of ePPP research should be codified in regulations with force of law and should be mandated, monitored, and enforced--in the same manner that oversight of select-agents, human-subject, and vertebrate-animals research is codified in regulations with force of law and is mandated, monitored, and enforced.

(5) Currently, the P3CO Committee operates with complete non-transparency and complete unaccountability. The names and agency affiliations of its members have not been disclosed, its proceedings have not been disclosed, and even its decisions have not been disclosed.

Oversight of ePPP research should be transparent and accountable.

(6) Currently, risk-benefit review of ePPP research excludes representation from the public, despite the fact that risks and benefits of ePPP research directly impact the public, making the public a stakeholder..

Oversight of ePPP research should include representatives of the public,

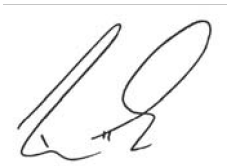
(7) Currently, responsibility for oversight of ePPP research is assigned to federal funding agencies and a federal department that perform ePPP research and/or that fund ePPP research. This constitutes an inherent conflict of interest.

Responsibility for oversight of ePPP research should be assigned to a single, independent federal agency that does not perform ePPP research and does not fund ePPP research.

Thank you for the opportunity to comment..

If you have any questions, please do not hesitate to contact me.

Sincerely,



Richard H. Ebright
Board of Governors Professor of Chemistry and Chemical Biology, Rutgers University
Laboratory Director, Waksman Institute of Microbiology

Submission Date: 9/18/22

Name: Nariyoshi Shinomiya

Name of Organization: National Defense Medical College (Japan)

Comment:

On the occasion of the NSABB conference of September 21, our research group believes as follows

The feeling of our research group is that the discussion at NSABB is being conducted based on a somewhat vague sense or philosophy.

We think it is necessary to examine as concretely as possible what has actually been done in the GOF research (to create ePPP) to date and what public health and medical issues it has contributed to. Without that, talking about benefits only in terms of principles may be just a theoretical discussion.

Taking COVID-19 as an example, there are clear public health contributions in areas different from GOF research, such as pathogen isolation, genome sequencing, mRNA vaccine technology, and drug repositioning. On the other hand, we think there is no clear evidence that the results of GOF research have contributed in any way to COVID -19 countermeasures.

Nor is there any verification (at least, we don't think it is explicitly stated to us, the general public) of what the governance of GOF research has been to date.

Without such verification, the discussion can only be a battle of ideology versus ideology among people with opposing views.

FYI, our recent paper on GOF research is as follows:

https://www.frontiersin.org/articles/10.3389/fbioe.2022.966586/full

Best regards,

Nariyoshi Shinomiya

On behalf of our research group

Submission Date: 9/20/22

Name: Tom Inglesby, Anita Cicero, Jaspreet Pannu, Marc Lipsitch, David Relman

Name of Organization: Assorted (refer to attachment)

Comment:

I hope all is well with you this week. Attached is a short response to the NSABB Preliminary Draft Findings and Recommendations that commends many of the good recommendations contained in the draft and expresses concern about issues not yet addressed in it. We have sent it to Gerry Parker and asked if he could send to the other NSABB members prior to the meeting tomorrow.

I hope you have a valuable and productive meeting tomorrow!

Additional Comment (attachment):

Response to the NSABB Document "Preliminary Draft Findings & Recommendations"

September 20, 2022

Dear NSABB members,

We are writing in response to the NSABB document *Preliminary Draft Findings & Recommendations* posted on the National Institutes of Health (NIH) website. In early July 2022, we and 29 other signatories (the 'Signatory Group') submitted a document titled *Recommendations to Strengthen the US Government's Enhanced Potential Pandemic Pathogen Framework and Dual Use Research of Concern Policies* to the NSABB, NIH, and White House.

The purpose of this letter is to commend several recommendations made in the draft NSABB document and to express serious concern about remaining gaps and shortcomings the Signatory Group believes should be specifcally addressed in the fnal NSABB fndings and recommendations.

We commend the NSABB for its recommendations to the US government (USG) to:

- ***Modify the defnitions of potential pandemic pathogens (PPP) and enhanced potential pandemic pathogen (ePPP)*** to include transmissible pathogens that have low or moderate virulence or low case fatality rate (CFR) as well as less transmissible pathogens that have higher CFR (thus expanding the defnition of what is included in the ePPP Framework).
- ***End the exclusion for surveillance and vaccine-related work.***
- ***Articulate specifc roles, responsibilities, and expectations for all institutions*** involved in the proposed research, including requiring local entities conduct ePPP reviews before submitting for USG review and requiring the same level of oversight throughout the course of the research (not only at the start).
- ***Develop more specifc information in articulating biosafety and biosecurity standards. · Develop principles and guidelines*** applicable to substantiating the claims that:
    1. There are no feasible, scientifcally sound alternative methods of obtaining the benefts sought in the research in a manner that poses less risk;
    2. Unnecessary risks have been eliminated and an overall assessment of remaining risks fnds that they are justifed by the potential benefts to society.
- ***Share a summary of key determinants and decisions*** resulting from USG review.
- ***Consider developing similar frameworks for pathogens*** that could pose severe threats to human health or food security via impact on animals and/or plants.

Despite these important recommendations in the NSABB's *Preliminary Draft Findings & Recommendations*, we are seriously concerned the document does not yet address a number of the most important recommendations from our July document, particularly 1b, 1c, 2c, and 3g. These recommendations can be summarized as:

- ***Broaden the ePPP Framework*** to incorporate the oversight of research that could enhance the virulence or transmissibility of any pathogen to produce an ePPP
- ***Within the ePPP Framework, establish oversight of sequence information*** about ePPPs, the risks related to computational methods for designing PPPs, and biosafety measures related to the synthesis of ePPPs, which would address the information hazards that are created as part of this work

- ***Distinguish between practical benefts and unsupported claims*** of beneft
- ***Improve transparency throughout the approval process*** by using a model such as Registered Reports to allow for the public to see risk-beneft assessments and any dissenting views prior to the research commencing.

In addition to the above, other critical shortcomings in current USG Policy that are not yet addressed in the NSABB's *Preliminary Draft Findings & Recommendations* are listed in our submitted recommendations as 2a, 2d, 3a-f, 4a-c, and 5. These can be summarized as:

- ***Articulate the risks that must be considered*** in the ePPP Framework process
- ***Defne the process for the "responsible communication of results"***
- ***Expand the stakeholders*** involved in the review and approval processes, and recuse those whose agency is funding or participating in the ePPP research
- ***Implement robust institutional health surveillance***
- ***Establish guidance regarding how to assess agents*** created during ePPP research
- ***Broaden the ePPP Framework to apply to non-federally funded research*** ·
  Require all USG agencies to implement the ePPP Framework
- ***Strengthen USG outreach to other governments*** to catalyze ePPP Framework and Dual Use Policy development
- ***Expand the types of experiments*** included in USG Dual Use Policy.

The recommendations noted above are highly important elements of a strong and clear governance framework for ePPP research and dual use research of concern (DURC) experiments. Incorporating these recommendations into the fnal NSABB document will help ***diminish the risk*** that US science could inadvertently initiate epidemics or pandemics while ***minimizing disruption*** of scientifc work that does not pose this risk; ***clarify the scope and decision-making*** process; and ***increase transparency*** around US policy and decision-making on these issues.

We remain very hopeful that as the NSABB considers the current draft and this additional feedback, these concerns (more fully articulated in the July 2022 recommendations document endorsed by 34 signatories) will be addressed in the fnal NSABB recommendations to the USG. We are greatly appreciative of the NSABB's careful consideration of these issues and value the importance of the constructive impact they will have on US policy.

Sincerely,

Tom Inglesby, MD
Anita Cicero, JD
Jaspreet Pannu, MD
Johns Hopkins University

Marc Lipsitch, PhD
Harvard University

David Relman, MD
Stanford University

Submission Date: 11/3/22

Name: Mary Lee Watts, Stefano Bertuzzi

Organization: The American Society for Microbiology (ASM)

Comment:

Dear Lyric and Cari,

The American Society for Microbiology (ASM) thanks the members of the NSABB and you for all your work to review and revise the P3CO and DURC policies. We appreciate the opportunity to provide additional thoughts on the process and specially, respond to the draft recommendations that were released and discussed at the September meeting. Attached is a letter with our views and additional recommendations, and if it would be helpful, we'd be glad to meet and discuss in greater depth.

Thanks for all you do.

Best,

Mary Lee

Additional Comment (attachment):

AMERICAN SOCIETY FOR MICROBIOLOGY

November 3, 2022

Lyric Jorgenson
Acting Assistant Director, Office of Science Policy
National Institutes of Health Bethesda,
MD DC

Dear Dr. Jorgenson:

The American Society for Microbiology (ASM), one of the oldest and largest life science societies with 30,000 members in the U.S. and around the world, supports and appreciates the work of the National Science Advisory Board for Biosecurity (NSABB). We thank you for your commitment to reviewing and revising policies governing Enhanced Potential Pandemic Pathogen (ePPP) research and Dual-use Research of Concern (DURC). The ASM recognizes the importance of cutting-edge research on human, animal, and plant microbes as well as our responsibility as scientists to minimize the likelihood that results of experiments with microbes of concern are misused or that these pathogens accidentally escape laboratory containment.

We are pleased to provide input on the preliminary draft findings and recommendations highlighted at the September 21, 2022 meeting and our perspective on publishing considerations discussed at the meeting.

Response to the Preliminary Draft Findings and Recommendations of the NSABB Working Group to Review and Evaluate P3CO Policy

ASM concurs with many of the proposed recommendations, and we thank you for considering the input ASM provided earlier this year to the Board and working group. We offer our strong support for recommendations three through five, which speak to the areas on which ASM has focused its attention.

Specifically, we concur with and wish to elaborate on the following:

- Recommendation 3: We agree that the federal process would benefit from more engagement from institutions and subject matter experts (SMEs), where investigators, institutional safety and review boards are the first line of oversight of proposed research. We believe that a strong “bottom up” approach to evaluating the risk-benefit of the research by those closest to the where it is taking place, coupled with “top down” oversight is most effective. Federal policies should complement local and institutional policies to ensure comprehensive and transparent oversight and review, which would avoid duplicative and lengthy reviews, or unnecessarily burdensome policies that create uncertainty and discourage investigators from proposing potentially life-saving research projects. For those institutional biosafety committees (IBCs) and review boards that do not have sufficient expertise to evaluate this research, having an NSABB-approved

cohort of experts who could assist in the review and also train reviewers would be helpful. Furthermore, a set of standard questions for use by all IBCs could be developed to ensure consistency. We should be cautious about placing additional burdens on an already highly regulated system. There is a lot that can be done at the laboratory and institutional level.

- Recommendation 4: We agree that principles and guidelines across U.S. government agencies should be developed that specifically address consideration of alternative approaches to riskier experiments, especially as science and technology advance, ensuring that risks at all stages of the research have been mitigated. We also acknowledge that this recommendation addresses expectations and standards for responsible communication of the research in question. Clear guidelines and expectations for communication between researchers, institutions, and federal funding agencies are imperative to avoid conflicts of interest and misunderstandings that have the potential to reduce the trust level not only between stakeholders, but also with the public. The Board might consider a special task force with subject matter experts to develop this plan, or these communications requirements could be considered a charge to the Board.

- Recommendation 5: We agree that increased transparency at all levels is essential to build trust and enable greater policymaker and public understanding of the value of DURC and its governing policies. In addition to accomplishing this through the development and release of an implementation plan and guidance, we agree that summaries of key determinants and reviews should be made available. Having said that, it is important to ensure this is done in a way that both protects scientists doing the research from being targeted maliciously, and those who are doing the evaluation. We think it is an imperative to consider a more regular NSABB meeting schedule, especially as critical situations arise (e.g. COVID-19 pandemic) as well as more regular reporting to Congress on the work of the Board and the policies. There is currently no requirement for regular review of the policies and currently no ongoing feedback loop to Congress. Given the recent COVID-19 experience, periodic reporting to Congress at an appropriate level of detail is needed to build trust and avoid misperceptions of secrecy., and policies should be reviewed and revised on a regular basis and as appropriate.

With respect to Recommendation two, ASM concurs with the inclusion of an “urgent” review path in this recommendation during a public health emergency or when national security is at risk. A thorough but “fast track” approach is essential in those situations. We also appreciate the need to ensure there are not blanket exemptions for certain activities and close potential biosafety and biosecurity loopholes, including surveillance and activities associated with vaccine development or production. However, we have concerns about the impact that potential overregulation of surveillance and vaccine development activities would have, and therefore we urge you to proceed carefully when considering means to strengthen oversight of this work. Experiments focused on antimicrobial escape mutants, vaccine escape mutants, and research to understand new mutations in field isolates are just a few examples of the types of research that are critical for public health and therapeutic development, and that fall in this category.

If surveillance is defined too broadly under these policies or stricter guidelines implemented incorrectly, we risk inhibiting our ability to detect novel pathogens as they emerge and known pathogens when they re-emerge in the U.S. and around the world and rapidly develop countermeasures to address them. In terms of vaccine development, we must be sure that work to understand vaccine “escapes” can be conducted and the use of lab models to ensure vaccines are effective against novel strains of pathogens is allowed. This is especially true when addressing seasonal and potentially pandemic influenza, and this work already is tightly regulated and conducted under strict biosafety parameters. For example, data derived from “gain of function research of concern” studies have been used to rapidly assess other recent emerging influenza strains such as A(H7N9) emergence in China, A(H5N1) in Egypt/Africa, as well as A(H5Nx) emergence in North America. “Gain of function” approaches which reveal pathways for evasion of therapeutics can also help with the timeliness rapid development of treatment guidelines for emerging antiviral resistance.

A One Health Approach is Needed

ASM is pleased to see the working group is giving strong consideration to animal and plant pathogens under an oversight framework. We believe strongly in a One Health approach, and we believe HHS and NIH have an important leadership role to play with other science agencies in the US. We understand there are roles beyond a specific agency for work on pathogens (for example, Department of Energy-funded super-computing; USDA funded work on animal and plant zoonoses; basic science through NSF.) and if we are to truly protect the U.S. and the world from the harmful impact of pathogens that target plants and animals, we must have analogous policies and processes for review that are harmonized with those already in place.

Publishing Considerations

As one of the largest publishers of microbial science research in the world, ASM has a rigorous process for assessing publications involving ePPP and DURC. We recognize that publishers play an important role in this space and we encourage harmonized activities that establish best practices in publishing. A case study published by the Visibility Initiative for Responsible Science (VIRS) in September 2022 highlighted ASM's multiple parallel mechanisms for flagging potential concerns in manuscripts, and reliance on extensive in-house expertise for its ultimate evaluations.[1]

ASM journals use multiple parallel mechanisms for flagging potential concerns in manuscripts and rely on extensive in-house expertise for its ultimate evaluations. We are fortunate to have former NSABB members in our membership who have formed the ASM Responsible Publications Committee (ARPC). The steps we take include the following:

- Manuscripts are automatically screened for keywords and phrases of concern, including the presence of agents on the US Department of Health and Human Services (HHS)' Select Agents and Toxins List (SATL).
- Manuscripts are also manually reviewed using a set of questions to evaluate their dual-use potential.
- If flagged, manuscripts are further reviewed by the editor-in-chief, and potentially also by the ARPC.

Importance of International Collaboration

In all of science, including in terms of support of enhanced potential pandemic pathogens research, ASM believes international collaboration is essential. We risk overregulating scientists in the U.S., and not providing leadership, training and mentoring to those in other countries seeking to establish biocontainment labs. Diplomacy is essential to success, and we encourage the NSABB and working group to consider these aspects in its continued deliberations and recommendations.

Thank you for your attention to our views. If we can be of further assistance or if you have any questions, please contact Mary Lee Watts, ASM Director of Federal Affairs at mwatts@asmusa.org or 571-228-8345. Sincerely,

Stefano Bertuzzi, PhD, MPH
ASM Chief Executive Officer

[1] Visibility Initiative for Responsible Science. "American Society for Microbiology Journals." *VIRS Case Study Collection, September 15, 2022.*