National Science Advisory Board for Biosecurity (NSABB)
Meeting Minutes

September 21, 2022
Virtual Meeting

Contents

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NSABB Members Present

Gerald W. Parker, Jr., D.V.M., Ph.D. (Chair)
Shannon Benjamin, M.S., M.B.A.
Kenneth Bernard, M.D.
Mark R. Denison, M.D.
Christina Egan, Ph.D.
Jacqueline Fletcher, Ph.D.
John D. Grabenstein, R.Ph., Ph.D.
Karmella Haynes, Ph.D.
Rachel Levinson, M.A.
Alex John London, Ph.D.
Nicolette Louissaint, Ph.D., M.B.A.
Syra Madad, D.H.Sc., M.Sc., MCP
Dennis Metzger, Ph.D.
Pamela A. Silver, Ph.D.

NSABB Members Absent

None

Meeting Overview and Goals

Lyric Jorgenson, Ph.D., Acting Associate Director for Science Policy, NIH

Gerald W. Parker, Jr., D.V.M., Ph.D., NSABB Chair, Associate Dean for Global One Health, Texas A&M University

Dr. Parker called the meeting to order at 1:00 p.m. ET. He noted that NIH would videocast the meeting and post it online. He explained that the NSABB is a federal advisory committee that provides, as requested, advice, guidance, and recommendations regarding biosecurity oversight of dual use research to the U.S. Government (USG). NSABB members bring a wide range of expertise and perspectives to bear, and the Board facilitates broad public engagement in the policymaking process.

After welcoming NSABB members and other attendees, Dr. Jorgenson noted that earlier in 2022, the USG tasked the NSABB with review of two key biosecurity policy frameworks governing life sciences research. The NSABB's charge includes evaluating and providing recommendations on the effectiveness of the current oversight framework for research involving enhanced potential pandemic pathogens (ePPPs), and the USG federal and institutional policies for the oversight of dual use research of concern (DURC). The NSABB formed two working groups to evaluate each policy framework.

Dr. Jorgenson said that the meeting would begin with a progress update from the working group charged with review of the Potential Pandemic Pathogen (PPP) Care and Oversight (P3CO) Policy. Later discussion would address oversight and governance, including responsible communication and the strengths and weaknesses of a potentially integrated P3CO and DURC oversight framework.

Ms. Young reviewed the conflict-of-interest (COI) policy. She reminded NSABB members that they are special Government employees and, as such, are subject to rules of conduct. Members are to disclose personal, professional, and financial COIs. Should an issue arise that could affect—or appear to affect—a member's interests, the member is requested to recuse himself or herself from the discussion.

Working Group Update: P3CO Policy Review

Gerald W. Parker, Jr., D.V.M., Ph.D., NSABB Chair; Associate Dean for Global One Health, Texas A&M University

Syra Madad, D.H.Sc., M.Sc., MCP, Senior Director, System-wide Special Pathogens Program, NYC Health + Hospitals

Dr. Parker presented background information on the working group's charge and their process to date. He turned to Dr. Madad, the working group's co-chair, to discuss draft findings and recommendations that have already been shared publicly.

Dr. Madad said that the Phase 1 charge to the NSABB is to evaluate and provide recommendations to the Office of Science Technology Policy (OSTP) and the Department of Health and Human Services (HHS) on the effectiveness of the current oversight framework for research involving ePPPs. The NSABB's P3CO evaluation should consider the policy's scope, in terms of preserving benefits of ePPP research while minimizing potential biosafety and biosecurity risks, supporting ePPP research internationally, and balancing considerations about security and public transparency when sharing information about research involving ePPPs.

The P3CO policy defines PPPs as pathogens that are (1) likely highly transmissible and likely capable of wide and uncontrollable spread in human populations and (2) likely highly virulent and likely to cause significant morbidity and/or mortality in humans. An ePPP is a PPP that results from the enhancement of a pathogen's transmissibility and/or virulence.

Dr. Madad summarized preliminary draft findings and recommendations.

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

The work group's considerations included whether the 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. Other considerations included experiences and lessons from the response to and recovery from the COVID-19 pandemic.

> **Recommendation 1.** Modify definitions of PPP and ePPP to include potentially highly transmissible pathogens having low or moderate virulence or case fatality rates, as well as pathogens that are less transmissible but have higher virulence or case fatality rates.

> **Finding 2.** The identification of ePPP research is informed by the current body of scientific evidence and knowledge, among other factors. The working group agrees that assessment should focus on the potential for an activity to create or involve ePPP, not the context in which the activity or modification is carried out.

The second finding focuses on the exclusion of certain types of activity from the P3CO framework. Per the USG P3CO policy, wild-type pathogens circulating in or recovered from nature are not addressed by the policy regardless of their pandemic potential. Additionally, pathogens resulting from modification of virulence or transmissibility of PPPs during surveilled activities (e.g., sampling and sequencing) and activities including developing or producing vaccines (e.g., generation of high-growth strains) are not considered ePPPs.

> **Recommendation 2.** The working group recommends that the USG reconsider the current exclusions for surveillance and vaccine development, so that all research activity that is reasonably anticipated as involving the creation, transfer, or use of ePPPs is subject to review under the P3CO policy framework.

The working group also recognizes the important role that surveillance and medical countermeasure development play in preparedness and response, and also recommends that processes be instituted for urgent review or evaluation of ePPP research that is determined to be critical for public health response or national security.

The USG P3CO policy requires federal departments and agencies to develop review mechanisms for identifying and overseeing ePPP research. The HHS PC3O framework outlines the roles and responsibilities of HHS funding agencies. Dr. Madad listed responsibilities of both HHS and funding agencies.

> **Finding 3.** 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 be revised to articulate specific roles, responsibilities, and expectations for investigators and institutions for or evaluation of research for potential involvement of ePPPs. 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 Regarding the PC3O Framework. The additional government-level review process outlined in the OSTP Policy Guidance was deemed generally appropriate. However, Sections 3.3 and 3.4 of the OSTP guidance, regarding risks and benefits, are inconsistent with similar policies as described in the *Belmont Report*. Section IV.C of the HHS PC3O Framework specifies extra care only at the department level for proposed research that is reasonably anticipated to generate pathogens covered by any of seven categories specified by the framework.

Finding 4 Regarding Implementation Directives. An implementation directive from HHS to its funding agencies and guidance from the federal funding agency to research institutions and principal investigators are lacking. This lack of directives and guidance has contributed to uncertainty and lack of clarity about the timing and expected requirements of the review process and about 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 development of research proposals.

Recommendation 4 Regarding PC3O Framework. Sections 3.3 and 3.4 of the OSTP P3CO Policy Guidance should be made consistent with the *Belmont Report.* The types of research outlined in the HHS PC3O Framework should be given extra care and consideration throughout the research proposal and review process by principal investigators, institutions, federal funding agencies—including those outside HHS—and at the federal department level.

Recommendation 4 Regarding Implementation Directives. Guidance and educational material should include:

- Steps, considerations, and criteria for identifying research that could involve ePPPs.
- Types of questions and information considered at each stage of review.
- Types of risks and benefits assessed (risk should be considered for the short and long terms and include review that considers potential consequences).
- The expected components of material evaluated (e.g., risk/benefit analysis, risk mitigation plan).
- Substantive information on biosafety and biosecurity standards, controls, and safeguards.
- Standards for review timelines under emergency and nonemergency conditions.
- Expectations and standards for responsible communication of research.

The USG should develop principles and guidelines that can be applied to substantiate that:

- There are no feasible, scientifically sound alternative methods of obtaining the benefits sought in a manner that poses less risk.
- Unnecessary risks have been eliminated and an overall assessment of remaining risks was done.

Finding 5. Regarding review process transparency and security, the HHS review group seems to have appropriate expertise, but the process needs to be more transparent. This

would enable a greater understanding of, and engender trust in, review and oversight processes for ePPP research.

Recommendation 5. The USG should take steps to increase transparency in the review process and consider sharing a summary of key determinants and decisions of its review.

Finding 6. 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 developing analogous policies and processes for additional review and oversight of research involving enhanced pathogens likely to pose severe threats to human health, food security, economic security, or national security by their impacts on animals and plants or their products.

Finding 7. Noting substantive overlaps between the intent and entities involved in implementing policies for oversight of ePPP research and DURC, the working group supports consideration of possible revisions that would incorporate ePPP research into the DURC oversight framework. It remains important that the principles identified earlier be included in a proposed consolidation of ePPP and DURC safeguards, and that review of oversight processes and risk mitigation measures be commensurate with the degree of risk posed.

Public Comments

Richard H. Ebright, Ph.D., Board of Governors Professor of Chemistry and Chemical Biology at Rutgers University and Laboratory Director at the Waksman Institute of Microbiology, noted defects in existing policy. These include lack of transparency, failure to review some ePPP risky experiments, exclusion of privately funded research from enforcement, lack of codified oversight and enforcement, and involvement of members of the public in review. The current situation involves a conflict of interest that could be resolved by giving oversight responsibility to a single, independent agency that does not oversee and fund research.

Anna Puglisi, M.S., Director of Biotechnology Programs and Senior Fellow at Georgetown University's Center for Security and Emerging Technology (CSET), said that differences in regulations lead to "ethical asymmetry" that could affect the speed of development and adoption of new technologies, push that development to other countries, and lead to misuse of new technologies. CSET has a nascent effort focused on mapping gain-of-function (GOF) research and DURC globally. CSET aims to create a set of signals to understand where there are studies involving GOF experiments, pathogens with pandemic potential, animal models, type of lab infrastructure, and genomic data. Understanding the types of GOF research, who conducts it, and how it is changing will help pinpoint anomalies and risks in research and development. CSET is also working on characterizing the state of current respiratory virus families using CSET open-source data holdings to determine trends.

Ms. Puglisi said that she could provide additional information to the board.

NSABB Discussion

Dr. Bernard noted that some public comments regarded issues that are broader than the working group's scope, such as the organization of the US governance, foreign involvement, and oversight of institutions that are not funded by the government. Many of these issues will be discussed by the NSABB in coming months. Dr. Bernard noted his concern that too much federal regulation will push currently unregulated research overseas. He added that the World Health Organization plans to draw up an international treaty to deal with future pandemics and worldwide health emergencies. Dr. Parker stressed the importance of understanding the scope of each of the parts of the charge related to the DURC and P3CO policies, not the entirety of the biosafety and biosecurity oversight framework in the U.S. He said that the working group's findings and recommendations are preliminary. A second group is working on issues noted by Dr. Bernard.

Dr. Denison noted his interest in CSET's work and methodology. He is concerned that public discussion of efforts regarding potentially worrisome research may have a chilling effect on investigators. Public comments addressed neither the impact of publishing bioinformatics analyses nor how risk and benefit are defined. Discussion has broadly applied the term "risk" to anything bad that may happen and "benefit" as having to be proven *a priori*. No evidence supports the idea that USG–supported pathogen research has led to the current pandemic.

Ms. Levinson said that some of the draft recommendations stem from discussions from stakeholders, particularly researchers whose proposed experiments underwent reviews. The stakeholders said that available guidance under the DURC policy is helpful. She urged consideration of a process that examines impact of compliance with the oversight policy, helps improve the oversight process, and allows changes as necessary. The community's feelings and suggestions are important, because no one can predict what research will be done in 10 or 20 years. Dr. Parker noted that some of that was discussed in a 2016 NSABB report.

Dr. Egan asked whether the working group had considered including documentation of the actual application forms and progress reports. Dr. Parker said that the message is that additional guidance is needed at all levels and that having checklists is not sufficient. More work must be done on specific guidance. The NSABB must advise the federal government on what to do. The DURC policy guidance is helpful. There must be something analogous for the P3CO, Dr. Parker added.

Dr. Denison said that compliance impact is an issue for very early scientific ideas, some of which have significant merit. The group was cautious about making recommendations about early or pre-submission review. An expanded biohazards section of the grant might help. Dr. Parker said that good models were proposed in DURC listening sessions for both working groups.

Dr. Metzger noted previous discussions about elevating local Institutional Biosafety Committee (IBC) responsibilities regarding ongoing research with pathogens. Discussions have suggested an initial and ongoing review of pathogen-related issues at the local level to help investigators understand the processes and potential mitigation steps that could be taken. Local IBCs would need guidance and oversight.

Dr. Parker noted that listening sessions raised the question of how to integrate top-down guidance, bottom-up accountability, and responsibility for ongoing oversight. Institutions and labs know their capabilities best. Laboratory and institutional leadership are essential to enhancing a culture of responsibility.

Dr. London said that unlike other research, PPP research can have effects that reach beyond the local institution and nation. The rationale for a more centralized top-down review is stronger, because the local community's risk tolerance may not be as important as uniform rules intended to mitigate the prospects of some types of release.

Dr. Bernard agreed on the need for oversight but added that oversight does not mean that primary control of proposals should lie with the federal government. The NSABB's original charter assigned local groups primary control of initial screening of DURC. The draft recommendations say that local groups must pick up the slack. Dr. Bernard noted a need for a strong, responsive federal body that gives expert advice to local groups and ensures that these groups' decisions are not counter to national or international good practices.

Dr. Parker said that resources, personnel, and harmonization are needed for proper oversight. He paused the meeting at 2:00 p.m.

Dr. Parker reconvened the meeting at 2:45 p.m. Dr. Parker welcomed speakers, saying their presentations and discussion would focus on managing biosecurity concerns when communicating research findings and would include discussion on the responsibilities of scientific investigators and journal publishers. He identified the session's goals as follows:

- Assess policies, procedures, and best practices when identifying, reviewing, and mitigating biosecurity concerns in research communications.
- Discuss the role and responsibilities of publishers and science communicators in balancing transparency and biosecurity concerns.
- Identify potential benefits and challenges with formalizing oversight roles and responsibilities in communicating DURC.

USG DURC Policies Review and Evaluation—Responsibly Communicating Research Methods and Results

Michael J. Imperiale, Ph.D., past and inaugural NSABB member; Professor of Microbiology and Immunology, University of Michigan

Richard Sever, Ph.D., M.A., Co-founder of Cold Spring Harbor Laboratory's preprint servers bioRxiv and medRxiv

Dr. Parker introduced Dr. Imperiale, noting that Dr. Imperiale has served on committees related to biosafety and biosecurity at the National Academy of Sciences, the National Aeronautics and Space Administration, and the Organization for Economic Co-operation and Development.

Dr. Imperiale recalled 10 years ago, when the NSABB discussed the H5N1 virus. That discussion involved consideration of research results that would present biosecurity threats, and it did not anticipate influenza transmission experiments. After discussing papers about such

experiments, and the finding that H5N1 viruses could become transmissible in mammals, the NSABB recommended that the research be reported but that the mutations that conferred that phenotype not be disclosed, lest those mutations be re-created and used for harm. There was pushback from journals and authors, and possible legal ramifications due to export control issues. As a result, authors submitted revised manuscripts after they were asked to clarify what they had and had not demonstrated and to clearly delineate the biosafety precautions they had taken.

The NSABB reconvened to consider whether revised manuscripts could be published after members had signed confidentiality agreements because of export control concerns. The NSABB heard from various interested parties and considered National Security Decision Directive 189, which says that, to the greatest extent possible, results of research should be freely disseminated. The NSABB voted unanimously to approve publication of one paper and, in a split vote, approved publication of the other, Dr. Imperiale said.

In response to these events, the American Society for Microbiology (ASM) established a committee on responsible publication, consisting of editors of journals likely to publish work related to H5N1. ASM added to its peer review form questions about whether research raises biosecurity questions. One ASM journal created a committee and process for considering specific biosecurity concerns. The process has always resulted in a decision to publish.

Dr. Imperiale added that the publication stage is too late to intervene, largely because the work has been peer-reviewed and reviewers have recommended publication. Additionally, committee members, who lack knowledge about biosecurity threats, discuss risks as hypotheticals. The committee must weigh the risk of not knowing enough about a natural threat versus risk of a bioterror event. Even if an organization decides not to publish research, it may be published or posted elsewhere.

Dr. Imperiale urged the NSABB to consider a more holistic and transparent process for considering whether research poses biosecurity risks, a process that may need to be different from reviews for typical NIH grants or contracts. Parameters of the work need to be evaluated at the beginning and on a continuing basis. Researchers must offer assurance that their work will be carried out safely, anticipate results, and have a plan for disseminating them from the beginning of their work, and restricted communication may be most appropriate. There must be consideration of a process for dealing with troublesome, unanticipated findings. Dr. Imperiale added that he hopes scientists will welcome scrutiny to show the public they are responsible.

Dr. Parker introduced Dr. Sever, noting that he is the assistant director of the Cold Spring Harbor Laboratory Press at Cold Spring Harbor Laboratory in New York and cofounder of the preprint servers bioRxiv and medRxiv.

Dr. Sever said that preprint servers for nonmedical fields allow dissemination of data from manuscripts that have not undergone peer review. Benefits include the opportunity to get feedback and visibility, as well as rapid dissemination of results so other scientists can build on them. Cold Spring Harbor launched bioRxiv and medRxiv to bring this approach to medical science. medRxiv has a separate server, because Cold Spring Harbor felt that a server for

medical science had a higher level of responsibility than other servers for basic biology do. bioRxiv and medRxiv have more than 200,000 papers and get 4,000 submissions per month. Seventy percent of papers on the servers are later published in journals.

Dr. Sever noted that preprints are becoming a fundamental part of the scientific communication process, but they also raise concerns about DURC. MedRxiv tries to be a responsible steward by noting that papers are not peer reviewed and what that means. Authors make declarations about COI, patient/participant consent, plagiarism, clinical trial registrations, and approval by institutional review boards (IRBs) or other ethics committees. Before going live, papers undergo a screening process to ensure they are not works of opinion, plagiarized, or dangerous. A "do no harm" rule ensures that papers do not make untrue statements or unwarranted challenges to established, proven treatments. Papers published in error can be withdrawn.

Dr. Sever noted several preprint servers and outlets that make papers available without any vetting. He questioned the effectiveness of journals at preventing dissemination of specific types of questionable research at a systemic level.

Dr. Sever encouraged educating researchers about responsible communication, as well as establishing international guidelines on responsible communication. He also encouraged better oversight by grant review bodies and institutions, as well as possible preregistration of research and papers that outline experiments before the research is done so that readers can compare the two, to enable a broader group of people to examine research plans. Funders should endorse preprint servers and journals they consider responsible outlets for dissemination.

Discussion

Dr. Metzger noted that animal research requires approvals at the beginning of the research process and urged using similar approvals for pathogens. He similarly stated the importance of getting approval for any changes to the experimental plan.

Dr. Imperiale noted that IBCs lack personnel to make such decisions and may come to differing conclusions and cautioned about putting "sand in the gears" by adding another level of scrutiny. Dr. Metzger said that IBCs could contract experts to help with decisions. Dr. Metzger added that the process he suggested could speed up grant proposals, because it would result in recommendations for mitigation.

Dr. Sever noted that his server will not post a paper about research on a potential intervention without a ClinicalTrials.gov ID. Determining how research from another country was funded is a challenge. Dr. Sever's servers have received about 20-25 papers about gain of function (GOF) that raised internal concerns, but only two or three of those papers were turned away due to the determination that they needed an additional level of scrutiny that Cold Spring Harbor's server could not provide.

Dr. Bernard noted that the fact that research that a journal or preprint server rejects will be published elsewhere has been a point of discussion related to local evaluation for 15 years, without effective solutions. He suggested that local IRBs or IBCs should deal with the issue and the NSABB should state how to get the appropriate expertise and support.

Dr. Sever asked for Dr. Imperiale's ideas about preregistration of research in clinical fields, such as social psychology. Preregistration involves publishing a research plan and broader scrutiny of it, which is useful if local expertise is lacking. Dr. Sever noted the possibility that a lack of expertise could mean that local bodies are unaware that a new technology could be used in a dangerous way. Dr. Imperiale said that preregistration has occurred for clinical trials, but not in this context.

Dr. Denison asked how risk and benefit can be assessed, especially for research on mutations associated with a specific mechanism or instances of viruses escaping from a compound. Dr. Imperiale noted that experiments cannot be halted just because researchers may get a resistant variant. But we must discuss what to do in such cases, he said. Dr. Sever said the answer to such questions may be different regarding the COVID-19 pandemic, with a constantly mutating virus, and regarding viruses that are much less widespread.

Dr. Imperiale asked whether it is better to have a group that issues a statement that it has considered biosecurity and biosafety issues and that specific research is worth pursuing, as opposed to having no review, a bad outcome, and loss of public trust in scientists. Dr. Denison suggested having a trans-institutional review group with a multicenter grant needing a multicenter review.

Dr. London asked Dr. Imperiale to identify a mechanism to ensure consensus about the value of a particular study. Dr. London asked who decides there is value in cases where there is disagreement about methods and whether lower-risk methods could accomplish the same objective. Dr. Imperiale said that he does not believe that role is appropriate at the local level, because different institutions' IBCs have different levels of risk tolerance.

Dr. Parker said that the main issue is how to combine top-down oversight with local responsibility. Dr. Metzger suggested that federally funded regional biosafety labs could be tasked with reviews if an IBC lacks expertise. Dr. Sever suggested that journals and institutions sign on to biosecurity policies, as they now do for policies intended to prevent reidentification of patients in clinical trials.

Governance Options for Oversight of DURC and PC3O

Renee Wegrzyn, Ph.D., Vice President, Business Development at Ginkgo Bioworks; member, National Academy of Science Standing Committee on Biotechnology Capabilities and National Security Needs

Marc Lipsitch, D.Phil., Professor of Epidemiology; Director, Center for Communicable Disease Dynamics, Harvard T.H. Chan School of Public Health

Sam Weiss Evans, D.Phil., M.Sc., Research Fellow, Harvard Kennedy School

Dr. Parker said that the session's goals were to:

- Identify potential strengths and weaknesses of an integrated DURC and PC3O framework.
- Discuss alternate governance approaches to managing research that poses potential biosecurity risks.

- Consider the pros and cons of various oversight frameworks.

Dr. Parker introduced Dr. Wegrzyn. Dr. Wegrzyn said she would present the industry perspective and in the context of questions shared with her before the meeting.

Regarding a question about identifying potential strengths and weaknesses of an integrated DURC and PC3O oversight framework, Dr. Wegrzyn said that engineering biology is becoming commonplace. The frameworks will be obsolete without considerations of emergent capabilities in definitions of governance and consideration of potential for dual use. Any guidance must be regularly pressure-tested because of future, unimagined DUR challenges.

In many cases, advances in engineered biology can be leveraged to reduce risk. The PC3O guidance has an underutilized part that asks whether a feasible, equally effective alternative method addresses the same question. Dr. Wegrzyn gave as an example an experiment on GOF that researchers say is difficult to recreate. She challenged that statement, suggesting examination of GOF experiments' goals and questions about pathogenicity the GOF experiments aim to answer. Dr. Wegrzyn argued that industry has foundry automated, high-throughput workflows that can answer many of these questions and reduce risk more quickly than traditional approaches.

Dr. Wegrzyn suggested that we find a new, better way to implement guidance. She recommended that we not rely on one agency to oversee industry and instead look to another part of government or industry. During her work on the Defense Advanced Research Projects Agency (DARPA) Safe Genes program, she realized that no clear regulations guided work in a way DARPA was comfortable with. In some cases, DARPA brought in external advisors to examine research teams' work and on a regular basis so investigators could make improvements.

Dr. Wegrzyn urged the NSABB to think about new ways to implement governance, noting that journals that lack people with biosecurity backgrounds may not recognize risks. The biosecurity research field is small enough that it could develop tools for looking for potentially concerning key terms and flag research even before it is conducted. In considering the pros and cons of a risk-based versus a list-based oversight framework, Dr. Wegrzyn said both would quickly become obsolete. She called for research about how to answer questions without working with dangerous viruses and new technologies to identify engineered threats and lab leaks. She noted that the Intelligence Advanced Research Projects Activity has a program that is intended to determine whether a genetic sequence is engineered and determines its intent.

Dr. Parker introduced Dr. Lipsitch. Dr. Lipsitch said he would comment on the PC3O draft recommendations, which he said he largely agrees with, though did note key points missing from the working group's draft:

- The draft misses oversight of research that leads to an ePPP but does not start with a PPP.
- The draft does not sufficiently address transparency.
- The general level of scrutiny for the potential benefits in the risk/benefit analysis should be higher, and the draft should be more specific.
- The draft does not address information hazards.

Dr. Lipsitch said that unifying the DURC and ePPP frameworks has advantages. Unification might make things simpler for investigators, encourage HHS to define each framework and clarify distinctions and common features, and promote sharing of best practices. Unifying the frameworks would involve systematically considering the biosafety and biosecurity issues separately and together.

Cons of unifying the frameworks include the potential for shifting focus too fully to biosecurity. ePPP research, although it can be considered a subset of DURC, raises biosafety issues that are not typical of all DURC. Dr. Lipsitch suggested unifying the frameworks and considering ePPP biosafety in addition to biosecurity considerations that ePPP research shares with DURC.

Dr. Parker introduced Dr. Sam Weiss Evans, D.Phil., M.Sc., a Research Fellow at the Harvard Kennedy School of Government who studies the history of security governance, said that biology and its role in society are redefined, so the NSABB has an opportunity to think about what constitutes elevated security concerns. He encouraged a system that is not fully top-down and that is based on collaboration and an understanding that security should be considered beyond just research that is directly in the scope of these specific policies. He suggested that the NSABB realize that all research is dual use, and he urged the NSABB to shift from a biosecurity governance system built for science to one that attends to wider concerns, including economics, health, and society. DURC policy should be complemented by a DUR policy with guiding principles. These principles include the recognition that all research can be used in ways that result in harms that will likely disproportionately affect disenfranchised communities. Research should be attentive to those communities' concerns. The principles should also note what types of oversight work for DUR are unknown, so that institutions that fund or conduct research can experiment with alternative approaches for spotting and addressing security concerns and share what they learn.

Discussion

Dr. Parker said that the field lacks the experimental basis to know what types of governance do and do not work. He asked Dr. Weiss Evans how science enterprises should acquire that knowledge. Dr. Weiss Evans pointed out that related experiments are already happening. The NSABB itself is an example, as are the Federal Bureau of Investigation (FBI) Weapons of Mass Destruction Directorate, which re-envisions the FBI's role related to biosecurity, and the iGEM Foundation's yearly competition, which allows recursion and iteration. Dr. Weiss Evans said it is difficult to counter strong institutional incentives to resist change.

Dr. London asked at what level judgments about the scientific merit of a specific methodology should be made. Dr. Lipsitch said Dr. London's question is difficult to answer. Considerations are different when the worst outcome is wasted money than if it is causing a pandemic. When lives are at stake, the justification must be stated in terms of lives saved and whether the experiment could be replaced with a safer alternative.

Dr. Wegrzyn mentioned engagement of affected communities. She urged rigorous definitions of risk and benefit and appropriate oversight on local review entities. Dr. Weiss Evan noted that the Department of Energy performed extensive reviews involving ethical, legal, and social issues before research was funded. In response to a question from Dr. Lyric Jorgenson, Dr. Wegrzyn said that at every level, stakeholders are responsible for understanding and communicating about research-related risk. She urged training to help the science workforce recognize risk. Coaching stakeholders about these issues should be standard practice.

Dr. Weiss Evans urged a change in the perception that everyone thinks that science does good, but rather that all research involves benefits and risks. There are many communities that do not believe that science does good and that have reason to mistrust it. He called for a change in culture that involves noting that no research is free of risk, making discussion of potential risks more acceptable. This does not happen in most U.S. research institutions.

Dr. Bernard urged the research enterprise to regulate itself, lest Congress do so. He believes that the term "DURC" should be changed and noted a lack of incentives for good biosafety and biosecurity practices. He asked the group how to incentivize scientists and institutions to do research safely. Dr. Lipsitch said that iGEM encourages young researchers to make biosecurity concerns part of their usual approach. Dr. Bernard asked how to align incentives among preprint servers, journals, and funders. He suggested that journals—even just a few highly respected ones—require certification that high-risk experiments have gone through extra validation.

Dr. Wegrzyn supported giving industry a role in developing biosecurity processes, because industry is also a funder, as is the venture capital community. Having a biosecurity plan and process could be a criterion for companies to get insurance. Dr. Weiss Evans said the steps Dr. Wegrzyn discussed should focus on biosecurity needs, including better screening and detection systems. Dr. Weiss Evans suggested lowering stakes for entities who are experimenting with using new governance approaches, because problems are inevitable and should be addressed within existing structures, lest they become political issues.

Dr. Lipsitch encouraged a discussion about how iterative approaches will work with how science is performed. Benefits are easy to determine, and risk is often hypothetical. He asked how to realistically propose experiments. Dr. Wegrzyn said an advisory board should look at experiments and be ready for the unexpected. Researchers should expect to revise their plans. Dr. Denison suggested that initial reviews involve an iterative plan presented by the scientist. It would explain how the work would proceed in possible scenarios. Dr. Lipsitch said the idea makes sense. Dr. Denison suggested developing a template like one used in drug development, featuring explanations of go/no-go scenarios.

Dr. Silver asked how to make policies work when the field of biology changes so quickly. She asked what happens when the field gets so good at predicting how biology works that experiments are not so necessary. Dr. Weiss Evans suggested training biologists to understand their work within a wider context. Dr. Silver said that her students are using artificial intelligence and machine learning. She predicted that some parties would think about making a pathogenic virus and that the formula for doing so would become more of a reality. Dr. Wegrzyn said that the ability to predict when research may have a bad outcome would be bolstered by proper

surveillance systems. Engineered biology's future requires figuring out how to communicate with the public.

Dr. Haynes, referencing previous discussion of incentives, said that researchers design projects according to what they expect in review. She urged funders to note what applications will ask about biosecurity and how it will be handled in reviews. Some parts of applications do not make science better and could be replaced with biosecurity-related questions. Dr. Weiss Evans, who noted that he is a reviewer, said that 5 years ago, he saw deficiencies in proposals' ethical, legal, and social information and would send them back, signaling that these issues are important. The review process is just one part of the wide research cycle that should pay attention to security concerns.

Closing Remarks and Adjournment

Dr. Parker thanked speakers and said that the NSABB would consider their input. Dr. Jorgenson noted that the board had heard important conversations that emphasized the need for oversight frameworks that can evolve, and how to incentivize a culture of responsibility to implement and sustain long-term changes.

Dr. Parker adjourned the meeting at 5:01 p.m.

Certification

I hereby acknowledge that, to the best of my knowledge, the foregoing Minutes and the following Attachments are accurate and complete.

This Minutes document will be considered formally by the NSABB; any corrections or notations will be incorporated into the Minutes.

Caroline E. Young -S

Digitally signed by Caroline E. Young -S
Date: 2022.12.14 16:52:35 -05'00'

Caroline E. Young, Sc.M. — Date
Executive Secretary
National Science Advisory Board for Biosecurity

Gerald W Parker, Jr.

15 December 2022

Gerald W. Parker, Jr., D.V.M., Ph.D. — Date
Chair
National Science Advisory Board for Biosecurity

Attachment I
NSABB Voting Member Roster

Chair

Gerald W. Parker, Jr., D.V.M., Ph.D.
Associate Dean for Global One Health
College of Veterinary Medicine &
Biomedical Sciences
Texas A&M University

Voting Members

Shannon Benjamin, M.S., M.B.A.
Associate Director, Research Safety BSL-3
Environmental Health & Safety
National Emerging Infectious Diseases
Laboratories
Boston University

Kenneth Bernard, M.D.
RADM, U.S. Public Health Service
(Retired)
Former Special Assistant to the President for
Biodefense, Homeland Security Council,
White House
Former Special Adviser for Health and
Security, National Security Council

Mark R. Denison, M.D.
Edward Claiborne Stahlman Professor of
Pediatrics
Professor of Pathology, Microbiology, and
Immunology
Director, Division of Pediatric Infectious
Diseases
Vanderbilt University Medical Center

Christina Egan, Ph.D.
Deputy Director, Division of Infectious
Disease
Chief, Biodefense and Mycology
Laboratories
Wadsworth Center
New York State Department of Health

Jacqueline Fletcher, Ph.D.
Regents Professor Emerita
National Institute for Microbial Forensics
and Food and Agricultural Biosecurity
Oklahoma State University

John D. Grabenstein, R.Ph, Ph.D.
Executive Director (Retired)
Global Medical Affairs
Merck Vaccine Division
Merck & Co., Inc.

Karmella Haynes, Ph.D.
Associate Professor
Wallace H. Coulter Department of
Biomedical Engineering
Georgia Institute of Technology and Emory
University

Rachel Levinson, M.A.
Executive Director
National Research Initiatives Knowledge
Enterprise
Arizona State University

Alex John London, Ph.D.
Clara L. West Professor of Ethics and
Philosophy
Department of Philosophy
Carnegie Mellon University

Nicolette Louissaint, Ph.D., M.B.A.
Senior Vice President of Policy and Strategic Planning
Healthcare Distribution Alliance

Syra Madad, D.H.Sc., M.Sc., MCP
Faculty, Boston University's Center for Emerging Infectious Diseases Policy & Research
Fellow, Harvard Kennedy School Belfer Center for Science and International Affairs
Senior Director, System-wide Special Pathogens Program, NYC Health + Hospitals

Dennis Metzger, Ph.D.
Professor and Chair, Immunology and Microbial Disease
Albany Medical College

Pamela A. Silver, Ph.D.
Elliot T. and Onie H. Adams Professor of Biochemistry and Systems Biology
Member, Harvard University Wyss Institute of Biologically Inspired Engineering
Department of Systems Biology
Harvard Medical School