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IDSA
Infectious Diseases Society of America

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[Submitted electronically to nsabb@od.nih.gov]

Samuel L. Stanley, MD
Chairman of the NSABB
Office of Science Policy
National Institutes of Health

IDSA Comments to the NSABB Working Paper on Evaluating the Risks and Benefits of Gain-of-Function Studies to Formulate Policy Recommendations

Dear Dr. Stanley,

The Infectious Diseases Society of America (IDSA) has closely followed the National Science Advisory Board for Biosecurity (NSABB) as it develops formal recommendations on how to assess the risks and benefits of gain-of-function (GOF) research of concern on pathogens with pandemic potential. IDSA members will be among the first responders to care for affected individuals in any disease outbreak, and will also lead research efforts to counter these disease threats. Accordingly, they are well positioned to understand the risks and benefits of these potentially dangerous experiments. Last summer, our society submitted recommendations for the NSABB as it worked with its contractor, Gryphon Scientific, to undertake a risk-benefit assessment (RBA) of the paused GOF research projects of concern, and then release its initial findings and recommendations.

IDSA has limited our comments today to those that apply to the NSABB's working paper, as it will shape the U.S. Government (USG) policy on the oversight of GOF research of concern. We applaud the NSABB's efforts to address IDSA's recommendations in the working paper, including its focus back to only the research of highest concern and its exclusion of seasonal influenza vaccine manufacturing and development. On the other hand, we are unified in our conclusion that the NSABB's draft findings and recommendations will not provide the appropriate guidance needed to develop a streamlined mechanism that provides appropriate oversight of the risk and benefits of GOF research of concern.

Below, IDSA offers specific recommendations to improve the areas of the working paper of greatest concern:

1. **Remove resistance to public health control measures as an attribute of GOF studies of concern**

IDSA strongly supports the NSABB's "key finding 1," that only a small subset of GOF research has risk that warrants an additional level of oversight." As IDSA stated in its earlier comments, a narrow focus only on GOF research of concern will

avoid an inadvertent regulatory capture of low risk research, which was not mentioned in the original White House description of research to be included in this deliberative process.

Consequently, IDSA believes the NSABB's proposed scope of GOF of concern, research that generates a pathogen that is highly transmissible, highly virulent, and resistant to public health control measures, may be unduly narrow. The limitations set forth on research in the NSABB document may fail to identify any GOF research for review and regulatory oversight, notably the types of experiments that sparked our current deliberation over the risk of GOF of research on pathogens with pandemic potential. Moreover both Gryphon Scientific and a number of panelist speakers at the January NSABB meeting concluded that public health control measures would have little ability to control a widespread outbreak of a highly virulent and transmissible pathogen. As stated in our earlier comments, IDSA again recommends that the NSABB focus oversight on GOF research that would be anticipated to combine both high pathogenicity and transmissibility in a pathogen; while escape from medical countermeasures is a concern, it is secondary to the above characteristics. This definition would capture the GOF experiments of greatest concern, and ensure that they are reviewed appropriately to assess their risk and benefits.

2. Exempt routine, responsible vaccine manufacturing from GOF oversight

The NSABB explicitly identifies the development and manufacture of seasonal influenza vaccines as not GOF research of concern. IDSA strongly agrees with this conclusion, understanding the critical importance of adapting and manipulating wild type influenza virus for improved growth in eggs and mammalian cell lines for vaccine manufacturing. However, our society believes that this explicit exclusion can be expanded to include all routine, responsible vaccine manufacturing activities. For example, the development of pre-pandemic and pandemic influenza vaccines uses standard methods and safety procedures that are widespread in the field. IDSA affirms that these routine activities pose little risk to the public, and play a critical role in public health preparedness.

3. Institute an independent standing board to review GOF of concern

The NSABB working paper concludes that "the U.S. government has effective policy frameworks in place for managing risks associated with life sciences research." IDSA strongly disagrees that the current policy frameworks, the USG Policy for Federal Oversight of DURC and the Department of Health and Human Services (HHS) GOF framework for H7N9 and H5N1 influenza, are sufficient to oversee GOF research of concern. For example, the USG DURC policy requires institutions to provide initial oversight of a GOF research project. As raised on several occasions by panelists at the January NSABB meeting, institutional biosafety committees (IBCs) vary widely in their expertise on assessing GOF research and lack transparent, easily accessible guidance to aid in these efforts. Often GOF research may reach a final line of review during submission for publication, where journal editors must take on the task of assessing the risk of publishing the findings; again they lack accessible guidance to ensure they provide appropriate review. In addition, the multiple frameworks of oversight for DURC, select agent research, recombinant DNA research, research that poses biosafety risks to human health or agriculture, research activities involving the shipment or export of infectious agents, and GOF research of concern create an often confusing regulatory environment that can impede scientific research, public health responses, and product development that are in the public interest.

Instead of building upon current oversight efforts, IDSA recommends the NSABB examine the formation of a standing advisory board for GOF research of concern. This board should be independent of GOF funding bodies and of those units within the government that may perform GOF research of concern, and could review GOF research of concern while also providing advice to investigators, IBCs, and journal editors. IDSA believes this board should include stakeholders with expertise in biosecurity, public health, and other relevant perspectives, and also have full access to the security information needed to appropriately assess GOF research. Given the security risks of the GOF research reviewed, it is likely that much of this board's activities may not be made publically available. Therefore, it is critical that the review process itself be as transparent as possible, with aspects that do not involve biosecurity being open to the public. While IDSA proposes that this board initially focus only on GOF research of concern, we do believe it could provide the template -or be expanded in scope-to replace current oversight frameworks in providing a streamlined and appropriate oversight of all DURC.

4. Develop recommendations to address biosecurity information risks

IDSA has noted that the NSABB working paper largely accepts Gryphon Scientific's conclusion that the information risk of GOF research of concern was minimal, stating that "most of the information of interest is already published, or non-GOF information relating to pathogens that are more attractive agents of harm is already available." IDSA asserts that while current GOF research information is already publically available, it is almost certain new research approaches, sequence information, and other data will be generated in the future that would pose novel, additional biosecurity information risks. IDSA strongly recommends that the NSABB reassess these risks, and either develop new recommendations that appropriately address them, and/or request input from other external science advisory groups that currently serve the Intelligence Community, with expertise in the life sciences and access to relevant classified information.

5. Strengthen working relationships with international GOF stakeholders

While the NSABB working report discusses the importance of global engagement and how U.S. policy will likely impact other global efforts, it does not make any specific recommendations on how to better engage international GOF stakeholders. IDSA understands that GOF research is proceeding in a relatively unimpeded manner in many countries outside of the US, but strongly believes that any USG activity would likely play a key role in the establishment of any international consensus on GOF oversight. We urge the NSABB to consider recommendations on how the USG can build strong working relationships with the international GOF stakeholder community. A robust global dialogue would allow the USG to observe the effectiveness of other GOF oversight efforts to better inform domestic USG policy; these stronger relationships will also be critical in making any progress towards international GOF oversight.

IDSA remains committed to ensuring that the broader scientific and science policy communities participates in efforts to guide GOF research appropriately. We hope the March National Academies of Science meeting on the NSABB's draft recommendations will include the perspectives of scientists, healthcare workers, policy-makers, ethicists, and representatives from the public that our society believes are critical in developing an appropriate oversight of GOF research of concern.

IDSA thanks the NSABB for this opportunity to comment, and looks forward to continuing to work with the U.S. Government and those who advise it to clarify the decision-making process on how and whether to undertake high-risk life science experiments. Should you have any questions or concerns about these comments, please feel free to contact Greg Frank, PhD, IDSA Program Officer for Science and Research Policy, at gfrank@idsociety.org or 703-299-1216.

Sincerely,

Johan S. Bakken, MD, PhD, FIDSA
IDSA President

About IDSA

IDSA represents over 10,000 infectious diseases physicians and scientists devoted to patient care, disease prevention, public health, education, and research in the area of infectious diseases. Our members care for patients of all ages with serious infections, including meningitis, pneumonia, tuberculosis, HIV/AIDS, antibiotic-resistant bacterial infections such as those caused by methicillin-resistant *Staphylococcus aureus* (MRSA) vancomycin-resistant enterococci (VRE), and Gram-negative bacterial infections such as *Acinetobacter baumannii, Klebsiella pneumoni*ae, and *Pseudomonas aeruginosa*, and, finally, emerging infectious syndromes such as Ebola virus fever, enterovirus D68 infection, Zika virus disease, Middle East Respiratory Syndrome Coronavirus (MERS-CoV), and infections caused by bacteria containing the New Delhi metallo-beta-lactamase (NDM) enzyme that makes them resistant to a broad range of antibacterial drugs.