Docket ID: EOP–2023–0001

Response to Request for Information (RFI, dated 09/01/2023) from the Office of Science and Technology Policy regarding Potential Changes to the policies for Oversight of Dual Use Research of Concern (DURC) and the Potential Pandemic Pathogen Care and Oversight (P3CO) Policy Framework

By Biosafety Now

Biosafety Now wishes to submit the following comments on potential changes to policies on DURC and to the P3CO Framework.

First, we strongly support the recommendations made by the National Science Advisory Board for Biosecurity (NSABB) on strengthening DURC and P3CO policies. Implementing the NSABB recommendations will strengthen oversight and will do so with no substantial costs and no substantial adverse impacts.

Urgent reform is needed in the federal oversight of DURC and enhanced potential pandemic pathogen (ePPP) research. Lapses in oversight of DURC and ePPP research may have caused the COVID-19 pandemic, and future lapses could cause future pandemics.

Second, we suggest additional changes to DURC policy to address shortcomings in implementation.

Currently, responsibility for review of DURC is assigned solely to investigators and their institutions. There are inherent conflicts of interest in a review process conducted solely by investigators and their institutions, and there is large institution-to-institution variation in the level of reviewer expertise (particularly national-security expertise) and in the level of reviewer due diligence. These realities necessitate additional review of DURC at the federal level. A federal agency that neither performs DURC nor funds DURC should oversee DURC review processes and review determinations to ensure compliance with policies. In addition, a federal agency that neither performs DURC nor funds DURC should conduct a federal-level review of the subset of DURC that poses highest risk: i.e., DURC with select agents and/or potential pandemic pathogens.

Third, we suggest additional changes to P3CO policies to address shortcomings in implementation.

Currently, almost no ePPP research undergoes the risk-benefit review mandated under the P3CO Framework. This is because federal funding agencies fail to forward ePPP research projects to the P3CO Committee for review. In the seven years since the P3CO Framework was implemented, only three ePPP projects underwent review by the P3CO Committee. Most ePPP projects–including the ePPP project on SARS-related coronaviruses at the Wuhan Institute of Virology that may have caused the COVID-19 pandemic–were not forwarded to and did not undergo review by the P3CO Committee. All ePPP proposals should undergo the risk-benefit review mandated under the P3CO Framework. All ePPP proposals automatically–without exceptions–should be forwarded to and 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 be added to grant and contract application forms and should automatically–without exceptions–trigger review.

Fourth, we suggest additional changes to P3CO policies to address shortcomings in operational transparency and accountability.

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. In addition, the P3CO operates without representation from the public, despite the fact that the risks and benefits of ePPP research directly impact the public, clearly making the public a stakeholder. Oversight of ePPP research should be transparent and accountable, and oversight of ePPP research should include representatives of the public.

Fifth, we suggest additional changes to P3CO policies to address shortcomings in assuring compliance with the Biological Weapons Convention (BWC).

The current P3CO Framework does not provide for review of projects for BWC compliance. The P3CO Framework should be changed to include an explicit requirement that the P3CO Committee review projects for BWC compliance, and correspondingly, an explicit requirement that the P3CO Committee have members with expertise in BWC compliance assurance.

Sixth, we provide the following numbered point-by-point responses to the questions raised in the RFI* (RFI questions in blue; responses in black)*:

1. The NSABB recommended that USG develop an integrated approach to oversight of research that raises significant biosafety and biosecurity concerns, including ePPP research and DURC (Recommendation 1). By merging the existing Federal DURC, Institutional DURC, and P3CO policies into a harmonized policy, a merged policy could potentially adopt the institutional applicability outlined in the Institutional DURC policy framework, making the following entities subject to a Revised Policy:

- U.S. Government departments and agencies that fund, sponsor, or conduct life sciences research.
- Institutions within the United States or its territories that both: Receive U.S. Government funds to conduct or sponsor life sciences research; and conduct or sponsor research that is within the revised scope, regardless of the source of the funding for the specific project.
- Institutions outside of the United States that receive U.S. Government funds to conduct or sponsor research that falls under the scope.

(a) What are the anticipated benefits and challenges of applying a Revised Policy, inclusive of both DURC and ePPP research, to the scope of entities outlined above?

We support the NSABB recommendation.

Anticipated benefits: All entities conducting research that raises significant biosafety and biosecurity concerns should be regulated. The NSABB recommendation would help accomplish this by extending regulatory coverage to all relevant entities that receive U.S. Government funds.

Anticipated challenges: None. Coverage will not impose substantial costs or substantial adverse impacts.

(b) What are the anticipated benefits and challenges of investigators and institutions having primary responsibility for identification of both DURC and ePPP research?

Anticipated benefits: It is appropriate for the *initial* identification and review of DURC and ePPP research to occur at the investigator and institution levels.

Anticipated challenges: It is not sufficient for the identification and review of DURC and ePPP research to occur *solely* at the investigator and institution levels.

As stated above, responsibility for review of DURC is currently assigned solely to investigators and their institutions. There are inherent conflicts of interest in a review process conducted solely by investigators and their institutions, and there is large institution-to-institution variation in the level of reviewer expertise, particularly national-security expertise, and in the level of reviewer due diligence. The inherent conflicts of interest and large institution-to-institution variation in review conducted at the investigator and institution levels necessitates additional review of DURC at the federal level. A federal agency that neither performs DURC nor funds DURC should oversee DURC review processes and review determinations to ensure compliance with policies. In addition, a federal agency that neither performs DURC nor funds DURC should conduct a federal-level review of the subset of DURC that poses highest risk: i.e., DURC with select agents and/or potential pandemic pathogens.

As also stated above, almost no ePPP research currently undergoes the risk-benefit review mandated under the P3CO Framework. This is because federal funding agencies fail to forward ePPP projects to the P3CO Committee for review. In the seven years since the P3CO Framework was implemented, only three ePPP projects underwent review by the P3CO Committee. Most ePPP projects–including the project on enhanced SARS-related coronaviruses in Wuhan that may have caused the COVID-19 pandemic–were not forwarded to and did not undergo review by the P3CO Committee. All ePPP proposals should undergo the risk-benefit review mandated under the P3CO Framework. All ePPP proposals automatically–without exceptions–should be forwarded to and 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 by investigators or institutions automatically–without exceptions–triggers review. For ePPP research, an analogous checklist of agents and activities should be added to grant and contract application forms and should automatically–without exceptions–trigger review.

2. Currently, the scope of the DURC policies is research that uses one or more of 15 listed agents or toxins and that produces, or is anticipated to produce, any of seven listed experimental effects. The NSABB recommended that the scope of research requiring review for potential DURC should include research that directly involves *any* human, animal, or plant pathogen, toxin, or agent that is reasonably anticipated to result in one or more of the seven experimental effects outlined in the DURC policy [6] (Recommendation 10.1).

The current list of 15 pathogens subject to DURC oversight is obsolete and incomplete. For reference, the list does not include any coronaviruses.

a. Considering the diversity of federally-funded research settings and portfolios, how would adoption of NSABB's Recommendation 10.1 affect policy implementation and research programs at the institutional level?

We support the NSABB recommendation. The list of pathogens subject to DURC oversight should be expanded and updated to include all human, livestock, and crop pathogens. The expansion of coverage will not impose substantial costs or substantial adverse impacts. This is because reviews are limited to research reasonably anticipated to result in one of the seven experimental effects outlined in the DURC policy, and only a small subset of research on pathogens satisfy this criterion.

b. Rather than including *any* pathogen within the scope of DURC review, one possible modification of Recommendation 10.1 would be to include DURC experiments that utilize:
i. HHS and Overlap Biological Select Agent and Toxins (BSAT) List [7] and/or
ii. Pathogen risk group (RG) classification of 3 or 4 [8] and/or
iii. Any pathogen where the conduct of work (*e.g.,* one of the DURC experimental categories) would require biosafety level 3 or 4 containment.
Would a modification of Recommendation 10.1, in line with the outlined scope of pathogens above, be useful for policy implementation? What specific benefits, challenges, and/or gaps are anticipated by this revised scope?

No. Such a modification would leave major gaps. A restriction to select agents would exclude all coronaviruses other than SARS-CoV-1 (i.e., would exclude SARS-CoV-2, MERS-CoV, and all other coronaviruses). A restriction to RG3 or RG4 pathogens would exclude all coronaviruses other than SARS-CoV-1, SARS-CoV-2, and MERS-CoV–and would have excluded the research in Wuhan on SARS-related coronaviruses that may have caused the COVID-19 pandemic. Likewise, a restriction to BSL-3 or BSL-4 pathogens would exclude all coronaviruses other than SARS-CoV-1, SARS-CoV-2, and MERS-CoV–and would have excluded the research in Wuhan on SARS-related coronaviruses that may have caused the COVID-19 pandemic.

c. Are there other risk-based approaches that would expand the scope beyond the current list of 15 agents and toxins provided in the DURC policy that would facilitate the identification of research that poses significant risks by investigators and institutions while not resulting in undue burdens?

No. Only a policy covering all human, livestock, and crop pathogens can identify all relevant research.

d. Given the possible revised scope of research requiring review for potential DURC, what modifications, if any, to the current DURC policy list of 7 experimental effects should be considered for a Revised Policy that captures appropriate research without hampering research progress?

None. The seven experimental effects are the relevant experimental effects.

3. A PPP is currently defined in the P3CO policy framework [9] as: “a pathogen that satisfies both of the following: 1. It is likely highly transmissible and likely capable of wide and uncontrollable spread in human populations; and 2. It is likely highly virulent and likely to cause significant morbidity and/or mortality in humans.” The NSABB recommended that the definition of PPP be modified to: (1) Likely moderately or highly transmissible and likely capable of wide and uncontrollable spread in human populations; and/or (2) Likely moderately or highly virulent and likely to cause significant morbidity and/or mortality in humans; and, in addition (3) Likely to pose a severe threat to public health, the capacity of public health systems to function, or national security” (Recommendation 2).

(a) How would the change in the definition of PPP affect the overall scope of a Revised Policy and its subsequent implementation?

We support the NSABB recommendation. The NSABB recommendation brings important clarification to the definition of PPP. This clarification will better align federal policies with the intention of the P3CO Framework, and will remove a loophole that has greatly undermined implementation of the P3CO Framework.

(b) One possible modification to the NSABB PPP definition is to specify a respiratory route of transmission within clause (1). Would that definition of PPP be an appropriate scope to mitigate risks and enhance effective implementation?

No. Limiting coverage to respiratory pathogens would eliminate coverage of important pandemic pathogens, including Ebola, Lassa, and Marburg viruses.

(c) Do you have additional suggestions to modify the PPP definition to mitigate the most significant risks not currently addressed and enhance effective implementation, while limiting negative or unintended consequences and burden on researchers, institutions, and the Federal government?

We support the NSABB recommendation.

(d) Are there characteristics related to human pathology, pathogen characteristics, or other features that would be helpful to clarify the intent of "moderately virulent"? Are there characteristics related to human pathology that would be helpful to clarify the intent of "moderately transmissible"?

The intent is clear from the text. The text operationally defines "moderately or highly virulent" as "likely to cause significant morbidity and/or mortality in humans." The text operationally defines "moderately or highly transmissible" as "likely capable of wide and uncontrollable spread in human populations." These definitions are clear and appropriate. Taken together–especially in conjunction with the third part of the definition, "likely to pose a severe threat to public health, the capacity of public health systems to function, or national security"–they include all potential pandemic pathogens (e.g., 1918 influenza virus, high-pathogenicity avian influenza viruses, SARS viruses, MERS viruses, smallpox virus, mpox virus, Hendra viruses, Nipah viruses, Ebola viruses, Lassa viruses, Marburg viruses, and the bacterium *Yersina pestis*), and exclude all other pathogens. Suggestions that the definition would cover almost all pathogens, and even would cover standard laboratory organisms such as *Escherichia coli*, are false.

4. A Government Accountability Office (GAO) report from January 2023 [10] recommended that the Department of Health and Human Services funding agencies should develop and document a standard to define "reasonably anticipated" to ensure consistency in identifying research that falls within scope of a Revised Policy. One possible definition of "reasonably anticipated" is: " `Reasonably anticipated' describes an assessment of an outcome that an individual with scientific expertise relevant to the research in question would expect this outcome to occur with a non-trivial likelihood. It does not require high confidence that the outcome will definitely occur and excludes experiments in which an expert would anticipate the outcome to be technically possible, but highly unlikely."

(a) Does this definition of "reasonably anticipated" provide additional clarity to ensure greater consistency in identifying research that falls within scope of the Revised Policy? What modifications to this definition (if any) would be most helpful?

We support the NSABB recommendation. The explanatory text recommended by the NSABB does not change the definition in the existing P3CO policy; it clarifies the definition in the existing P3CO policy. Specifically, the explanatory text recommended by the NSABB would prevent misinterpretations of the definition in the P3CO policy that construe "reasonably anticipated" to mean "certain" or "nearly certain". Such misinterpretations are inconsistent with the letter of the P3CO policy, the spirit of the P3CO policy, and the discussions in the deliberative process that led to the P3CO policy. Nevertheless, the absence of explanatory text in the current P3CO policy has enabled some to advance these misinterpretations.

With the explanatory text recommended by the NSABB, the "reasonably anticipated" standard of the P3CO policy will be as clear as the "reasonable person" standard widely used in US civil law.

5. NSABB recommends the removal of blanket exclusions for research activities associated with surveillance and vaccine development or production for research with ePPPs (Recommendation 3).

(a) Should exemptions for certain activities be included in a Revised Policy?

No. Any exemption would create a loophole that undermines the P3CO policy. Eliminating the exemption for research activities associated with surveillance and vaccine development or production would prevent misinterpretations of the P3CO policy that construe the exemption to apply to entire *projects* relevant to surveillance or vaccines even when the ePPP *research activities* in those projects are not relevant to surveillance or vaccines. Such misinterpretations are inconsistent with the letter of the P3CO policy, the spirit of the P3CO policy, and the discussions in the deliberative process that led to the P3CO policy. Nevertheless, the absence of explanatory text in the current P3CO policy has enabled some to advance these misinterpretations.

(b) What are the benefits and drawbacks of including exemptions for domestic and international pandemic preparedness, biosafety, biosecurity, and global health security?

There would be no benefits, and there would be major drawbacks. Any exemption would create a loophole that undermines the P3CO policy. Eliminating the exemption for research activities associated with domestic and international pandemic preparedness, biosafety, biosecurity, and global health security would prevent misinterpretations of the P3CO policy that construe the exemption to apply to entire *projects* relevant to these subjects even when the ePPP *research activities* in those projects are not relevant to these subjects. Such misinterpretations are inconsistent with the letter of the P3CO policy, the spirit of the P3CO policy, and the discussions in the deliberative process that led to the P3CO policy. Nevertheless, the absence of explanatory text in the current P3CO policy has enabled some to advance these misinterpretations.

(c) If exemptions are included, how could they be bounded to maximize safety and security and minimize negative impact on domestic and global public health including outbreak and pandemic preparedness and response? For example, would vaccine research and development activities be unjustifiably impeded if the current P3CO policy framework exemption for “Activities associated with developing and producing vaccines, such as generation of high growth strains” was either removed completely or modified to “Research on PPPs directly associated with testing and/or producing vaccines, such as generation of high growth strains”?

No exemptions should be included.

Thank you for the opportunity to comment. If you have any questions please do not hesitate to contact us.

Sincerely,

Biosafety Now
info@biosafetynow.org

Biosafety Now (https://biosafetynow.org/) *is a US-based non-profit organization of science and technology research professionals, policy professionals, community activists, and members of the public who are concerned about the risks that pathogen research poses to the public.*