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OFFICE OF THE VICE PRESIDENT – RESEARCH AND INNOVATION

OFFICE OF THE PRESIDENT
1111 Franklin Street, 11th Floor
Oakland, California 94607-5200

Submitted through: https://www.regulations.gov

October 16, 2023

Stacy Murphy
Deputy Chief Operations Officer/Security Officer
Office of Science and Technology Policy
Executive Office of the President
1650 Pennsylvania Avenue
Washington, D.C. 20504

RE: UC Comments in Response to OSTP's Request for Information to Proposed Changes to DURC and P3CO Policies [Docket ID (EOP–2023–0001)]

Dear Deputy Chief Operations Officer/Security Officer Murphy:

I write on behalf of the University of California (UC) system in response to the Request for Information (RFI) on "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" published in the Federal Register on September 1, 2023.[1] UC is comprised of ten research-intensive campuses, six medical schools, and three affiliated U.S. Department of Energy national laboratories.

Endorsement of COGR Comment Letter

UC endorses COGR's Comment Letter[2] and shares its concerns about the consequences of adopting a "risk-based" approach, instead of the current "list-based" approach and shifting entirely the burden of DURC and ePPP risk assessments to institutions.

General Comments

UC appreciates OSTP's effort to update the existing DURC and P3CO policies and address the recommendations in the report from the National Science Advisory Board for Biosecurity

[1] 88 Fed. Reg. 60513 (Sept. 1, 2023).
[2] Letter from COGR to OSTP (Oct. 13, 2023), *available at* https://www.cogr.edu/sites/default/files/final%20response%20to%20DURC%20RFI%20Oct%2013%202023%20v2%20(003).pdf.

(NSABB), *Proposed Biosecurity Oversight Framework for the Future of Science*.[3] UC recognizes the need to "ensure [the U.S. biosafety oversight system] effectively address[es] existing and emerging safety and security concerns while continuing to support scientific progress and innovation." UC is committed to ensuring biosafety and biosecurity when working with high-risk pathogens and following all Federal policies to protect public safety and national security from potential harms from life science research.

As current biosafety programs (e.g., FSAP, DURC, and P3CO) have similar overall goals with respect to high-risk pathogen research, UC supports the combination of these programs into a single regulatory program. Doing so should increase efficiency and otherwise help to reduce the burdensome nature for administration and implementation of these policies.

Federal policies must be balanced with the equally important need for institutions to conduct biomedical research. This need came to prominence during the recent SARS-CoV-2 pandemic. Institutions were looked upon to provide urgently needed research to understand the disease mechanisms of the virus so effective treatments and vaccines could be developed quickly. To the possible detriment of this type of ongoing research, we believe some of the individual proposed policy changes may place an inordinate burden on local Institutional Review Entities (IREs) and Institutional Biosafety Committees (IBCs), inadvertently slowing research when urgently needed, and undoing the efficiencies gained by having a single regulatory framework. Any combined biosafety and biosecurity framework should avoid this.

Furthermore, Federal government agencies (e.g., NIH, CDC, etc.) should also play an important role in the risk assessments for potential pandemic pathogens and to establish appropriate safety procedures going forward. We suggest these agencies provide support to local IREs and IBCs for particularly complicated situations.

Specific Comments

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

Giving institutions primary responsibility for identification of DURC and ePPP research would give them more freedom and could allow for a single review process for DURC and ePPP research. However, this responsibility would also place significant burdens on institutions when combined with the contemplated change in scope mentioned in Question 2 (discussed below). Institutions would be required to perform significantly more risk assessments for research involving an unlimited number of pathogens, including those currently considered low-risk.

[3] National Science Advisory Board for Biosecurity (NSABB), Proposed Biosecurity Oversight Framework for the Future of Science (Jan. 2023), *available at* https://osp.od.nih.gov/wp-content/uploads/2023/01/DRAFT-NSABB-WG-Report.pdf.

As an alternative, U.S. Department of Health and Human Services funding agencies would assess the risks of the research and the potential for DURC as part of the proposal review process. This would ensure uniformity in implementation of the policy, including in the assessment of whether any of the experimental effects in the DURC policy may be reasonably anticipated.

1(c) What types of resources or tools would be useful for researchers and institutions to determine if their research falls into a revised policy scope that is risk-based rather than list-based, and adequately conduct risk assessments to identify DURC and ePPP research?

To help IREs and researchers manage the significant increase to burden associated with reviewing all research involving any pathogen or toxin, the U.S. Government should provide clear guidance and training, including examples, of what needs to be reviewed and how to conduct these risk assessments. The guidance should include methods to quickly identify research with greater risk of involving DURC and ePPP and equally important, to identify and promptly exclude the review of low-risk research. Ideally, NIH, CDC, or other federal agency or office could provide specific advice to institutions and readily answer questions from institutions.

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).
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?

UC is very concerned with expanding the scope of DURC to include "*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." (emphasis added). We view this approach as overly broad and would subject a boundless and undefined number of pathogens and toxins to institutional review. Reviewing a much broader scope of research may divert from review efforts on pathogens and toxins of greatest concern.

In addition, the significant increase in DURC reviews would place a tremendous burden on principal investigators (PIs), Institutional Review Entities (IREs), and Institutional Contacts for Dual Use Research (ICDURs), and biosafety offices. First, PIs are increasingly tasked with performing a myriad of compliance and administrative tasks that encroach on their research time. Adding an institutional review hurdle for PIs working with *any* pathogen simply increases this burden, even for low-risk research. Second, this would greatly increase the workload for IREs. The significantly increased number of reviews would make it even harder to recruit IRE members, especially as they do not receive any compensation for this work. Finally, ICDURs and biosafety

offices would bear the brunt of the increased volume of reviews. A correlative increase in funding to biosafety offices would be necessary to meet the additional workload. However, the cap in the administrative cost component of negotiated indirect cost rates makes it virtually impossible to adequately cover increased funding needs.

There already exists a plethora of publications and information about many pathogens that are not currently subject to DURC and are of lesser concern, such as *Salmonella*. An undefined scope of DURC would unnecessarily subject such pathogens to restrictions and would only hamper biomedical research in them.

2(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 and/or*
- *ii. Pathogen risk group (RG) classification of 3 or 4 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?

UC recognizes that there may be a need to expand the current list of 15 DURC agents and toxins. For the reasons discussed under 2(a), UC would support maintaining a list-based approach to identify pathogens subject to DURC review, such as the one under subsection i. The DURC policy should provide a clear mechanism to add an agent or toxin to the DURC list, one that identifies specific risks associated with the agent or toxin that explains why it is being added. While Subsection iii. narrows the field from all pathogens, it still lacks the clarity of a defined list and presents the same problems as discussed above.

UC supports the comments submitted by the Centers for AIDS Research (CFAR) as to how modifications ii. and iii., would negatively impact AIDS research. These modifications would make human and simian immunodeficiency viruses (HIV and SIV, respectively) and tuberculosis (TB) subject to DURC review despite no documented incidents to warrant the additional oversight.

2(e) What resources or tools would be valuable to assist with implementation of a DURC policy with a scope that is revised to include more than the current list of 15 agents and toxins?

As discussed under Section 1(c), should the scope of the DURC policy expand beyond the current 15 agents and toxins due to a "risk-based" approach, then institutions would need clear guidance, including examples, of how to conduct such risk assessments.

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?

Currently, the P3CO excludes pathogens from the definition of ePPPs for research involving surveillance activities or activities associated with developing and producing vaccines. The SARS-CoV-2 pandemic demonstrated the need to quickly share research on surveillance and vaccine development. If these exclusions are removed, UC recommends the Federal government provide an alternative mechanism or clear guidance on how research associated with surveillance and vaccine development or production can be disseminated quickly in a future public health crisis.

6. NSABB recommends that continued assessment of the risks and benefits associated with advances and applications of bioinformatics, modeling, and other in silico experimental approaches and research involving genes from or encoding pathogens, toxins, or other agents must inform future evaluations of the scope of research oversight policies to help ensure that associated risks are appropriately identified and managed. (Recommendation 10.2). This type of research is not currently included in the DURC and ePPP oversight policies.
(a) Is there a subset of such in silico research that should require risk assessment and review in a Revised Policy, and if so, how should this research be defined so that the Policy captures the appropriate research without hampering activities with limited biosecurity risks?
(b) One possible way to define this category of in silico research within a Revised Policy would be to include experiments that are reasonably anticipated to:
"(i) Develop in silico models that directly enable the predictive design of an enhanced potential pandemic pathogen or novel pathogen or toxin covered under a Revised Policy that could be constructed via genomic editing or de novo synthesis; and/or
(ii) Develop a dataset(s) connecting nucleic acid or amino acid sequences with experimentally-determined pathogenic functions in a manner sufficient to enable the development of in silico models described in (i)."

Although a very helpful technology, *in silico* models may not be able to predict all potential risks associated with studying an aspect of a particular agent nor predict functions of newly discovered or highly variable genes, especially if this discovery research is carried out on a new emerging pathogen with limited or no additional information. Following the development of the *in silico* model, the approach requires confirmation within a living organism. Upon introduction into a host, a pathogen may behave differently than expected based on the *in silico* model, which may require additional risk assessment by the IRE. Therefore, relying on *in silico* models to fully predict risks or gene functions associated with the modification of a pathogen may not suffice.

Evaluating *in silico* models will dilute institutional resources and take focus away from evaluating work with biological organisms. It is better to maintain focus on DURC with actual biological organisms.

If *in silico* research must be evaluated, note that IREs rarely have members who have subject matter expertise in computational science. If *in silico* research were subject to risk assessment by the IRE or an IBC, OSTP must provide clear, detailed guidance to institutions and researchers as to what must be reviewed and how expected risk assessments must be conducted. OSTP should provide extensive training to IREs on the conduct of reviews and provide detailed decision trees that they can employ. Finally, OSTP should designate dedicated points of contact that would be readily available to respond to institutional queries and provide detailed and specific guidance.

Conclusion

UC greatly appreciates OSTP's invitation to comment and participate in the discussion of the future of the DURC and P3CO policies. We understand the need to maintain an effective biosafety and biosecurity oversight system to protect public health and national interests. We also appreciate the challenge of updating this system to match the evolving risks that accompany research with pathogens and toxins. To be effective though, the policies must be clear as to how institutions should devote their efforts. Our comments seek to highlight proposed modifications that would dilute those efforts and provide suggestions that would enhance them.

The RFI seeks feedback on many significant changes to these policies and the biosafety and biosecurity framework as a whole. There are many researchers and staff at UC that are directly impacted by these policies. Unfortunately, the 45-day comment period was not sufficient to consult with all the impacted stakeholders to develop more improvements to the DURC and P3CO policies. We strongly encourage OSTP to continue engaging with researchers and institutions as it updates the DURC and P3CO policies, such as through open forums or additional requests for information.

Thank you for the opportunity to comment. If you have any questions concerning these comments, please contact Timothy Miller, Research Policy Manager, at Timothy.Miller@ucop.edu.

Sincerely,

Lourdes G DeMattos

Lourdes DeMattos
Director
Research Policy Analysis and Coordination
University of California, Office of the President