The GEU IACUC and IBC should work collaboratively with each other and the CRO to address both the concerns of the GEU IBC and the researcher to ensure compliance with federal regulations and internal policy while recognizing the priority of the COVID-19 related research. ❐

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References
1. Institute for Laboratory Animal Research. *Guide for the care and use of laboratory animals.* 8th Ed. (Washington, D.C., National Academies Press, 2011).
2. Office of Laboratory Animals, National Institutes of Health. Frequently Asked Questions. PHS Policy on Humane Care and Use of Laboratory Animals. *D. Protocol Review. 8.* Available from: http://olaw.nih.gov/guidance/faqs
3. Holthaus, K., Goldberg, D. & Connelly, C. et al. *J Clin Transl Sci.* **4**, 96–101, https://doi.org/10.1017/cts.2019.431 (2020).

It takes two to MOU

When evaluating this scenario, OLAW provides clear guidance on IACUC oversight of interinstitutional collaborations. Institutions should have formal written contracts outlining the responsibility for "offsite animal care and use, animal ownership, and IACUC review."[1] If the research is sponsored by federal funding, the *NIH Grants Policy* further requires the agreement to incorporate applicable PHS Policy requirements for review and approval of proposed animal activities, significant changes, and semiannual IACUC program review.[2] The *PHS Policy* requires that the research be conducted within an assured institution, whose IACUC would have purview.[3,4]

If both Great Eastern University (GEU) and the CRO are assured, Dr. Mayfield is correct in that there is no federal requirement for dual IACUC review[4] and it becomes undue university-level regulatory burden. However, the institutional IBC is a separate entity with a different role, as defined by the *NIH Guidelines*. Regulatory guidance involving interinstitutional IBC collaborations is lacking, and Mayfield should not assume that OLAW's policy applies. The *NIH Guidelines* state that "each institution (and the [IBC] acting on its behalf) is responsible for ensuring that all research… conducted at or sponsored by that institution is conducted in compliance with the *NIH Guidelines*."[5] Since GEU is sponsoring the study, its IBC remains responsible for oversight in a manner in which it feels is most appropriate. One could argue that because GEU does not have BSL-3 facilities, its IBC may lack the necessary expertise to perform a proper risk assessment of the proposed activities at the CRO; however, that is irrelevant because it is within GEU IBC's authority to halt the study.

Extending from these observations, it is clear for this scenario that the establishment of a Memorandum of Understanding (MOU) between GEU and the CRO is the most appropriate path forward. Prior to its finalization, the MOU needs to not only clarify the roles and responsibilities for the project, both administratively and clinically, but it also needs to assuage the fears of GEU's IBC. Although rooted in caution, the IBC's concerns of an escaping mouse need to be critically evaluated with a thorough risk assessment. In the authors' experience, mice escaping from their cages is a rare event, and even rarer then for the animal to escape the room and subsequently escape from the facility. Moreover, due to infrastructure in place in ABSL3 facilities, such an escape is even less likely to occur. And finally, although the mouse can be infected with the SARS-CoV-2, is it plausible that it could transmit the virus to other animals? Or worse yet, people? This fact is critical for proper risk assessment, although the authors recognize an answer may not be apparent. The scenario in which a mouse may escape the facility and become the murine analogue of "Typhoid Mary" of SARS-CoV-2 appear infinitesimal, and this should become apparent through a thorough risk assessment. The findings of this risk assessment should be noted in the MOU between the two institutions. ❐

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References
1. Institute for Laboratory Animal Research. *Guide for the care and use of laboratory animals.* 8th Ed. (Washington, D.C., National Academies Press, 2011)
2. Office of Extramural Research, National Institutes of Health. *NIH Grants Policy Statement* Chapter 15.2.1 (IV.B.2.)
3. Office of Laboratory Animal Welfare, National Institutes of Health. *Public Health Service Policy on the Humane Care and Use of Laboratory Animals*
4. Office of Laboratory Animals, National Institutes of Health. *Frequently Asked Questions. PHS Policy on Humane Care and Use of Laboratory Animals. D. Protocol Review. 8.* Available from: http://olaw.nih.gov/guidance/faqs
5. NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules.

Did someone say MOU?

The sudden emergence of the SARS-CoV-2 coronavirus pandemic has had a profound global impact. As the virus continues to spread, the search for a vaccine is imperative in mitigating the virus' devastating clinical and economic effects. Due to the rapid transmission rate of the virus, biomedical research around the world has significantly increased during this crisis to develop prevention and treatment strategies. Researchers such as Dr. Marty Mayfield of Great Eastern University have stepped forward to develop these potential clinical innovations and therapeutics targeting the SARS-Cov-2 coronavirus.

To conduct SARS-CoV-2 research, Mayfield needs access to an ABSL3 facility[1]; Great Eastern does not have this capacity, so he has partnered with a CRO to perform the SARS-CoV-2 mouse experiments. He is an experienced scientist that has successfully worked within Great Eastern's IACUC and IBC policies in the past. Given the level of necessary collaboration between Great Eastern University and the CRO, it is paramount that both institutions come to an

agreement regarding their respective roles within the scope of the research project.

Without fully knowing who is providing funding for the research, it is difficult to determine each institutions' specific responsibilities. Regulatory oversight hinges on answers to questions such as who is the actual grantee and which institution owns the animals. According to its Rules of Accreditation, AAALAC International follows animal ownership to determine who is responsible for animals at an offsite program[2]. The grantee institution in this case is Great Eastern; the animals are thus owned by them. Assuming the funding is from the National Institutes of Health (NIH), the animal work is also covered by the Public Health Service (PHS) Policy.

As the work utilizes a recombinant mouse-adapted strain of SARS-CoV-2, an IBC must review Mayfield's proposed work for compliance with the NIH Guidelines (Section IV-B-2-b-(1))[3]. Coverage by NIH Guidelines *"includes research collaboration or contractual agreements"* (Section I-C-1-a [2]). The ABSL3 work constitutes a contractual agreement or subaward[4]; NIH Guidelines must be met at the CRO. An IBC may, based on its home institution's policies, allow oversight of the work by a second IBC (i.e., at the CRO).

We postulate that the difference in approvals between the CRO and Great Eastern IBC stems from differences in either institutional risk tolerance, a lack of knowledge regarding the CRO's ABSL3 biosafety features, or both. This risk is not without merit. Failure to adequately identify and mitigate biosafety risks at the CRO could jeopardize both human health (e.g., escaped mouse) and any further NIH funding *for the grantee* (Great Eastern). To reduce the university's institutional risk, Great Eastern's IO and its responsible official (often, but not always the same individual) should create a memorandum of understanding (MOU) between the university and CRO. Without such an MOU, Mayfield's research cannot proceed. The MOU should clearly state that the onus of all IACUC and IBC regulatory oversight and compliance lies with the CRO. In this way, we believe that University risk is mitigated while allowing Mayfield's valuable SARS-CoV-2 work to proceed. ❐

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References

1. Office of Science Policy, National Institutes of Health. *FAQs – Interim Laboratory Biosafety Guidance for Research with SARS-CoV-2 and IBC Requirements under the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* https://osp.od.nih.gov/biotechnology/interim-lab-biosafety-guidance-for-research-with-sars-cov-2/ (last accessed 10/20/2020)
2. AAALAC International. *Rules of Accreditation. Section 1. Definitions: Animal Ownership*. July 2020. https://www.aaalac.org/accreditation-program/rules-of-accreditation/
3. NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules
4. National Institutes of Health. Dec 2019. NIH Grants Policy Statement.

A WORD FROM OLAW

In response to the issues posed in this scenario, the National Institutes of Health – Office of Laboratory Animal Welfare (NIH–OLAW) provides the following clarification with the assumption that the research is funded by NIH:

In this scenario, two institutions are partnering to conduct SARS-CoV-2 coronavirus research. There are differences of opinion between the Institutional Biosafety Committees about the safety conditions necessary for conducting the research with infected mice. The question asked is what regulatory requirements must the IACUC follow.

As mentioned by other reviewers, NIH grants policy requires that when a grantee institution collaborates with another organization, the primary recipient of the grant funds is accountable for the performance of the project and all other obligations specified in the grants policy[1]. It also states that the primary recipient is responsible for including these requirements in its agreements with collaborating organizations"[1,2].

In addition to the NIH grants requirements above, the institution must adhere to the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*. The Institutional Biosafety Committee (IBC) must ensure that research conducted at or sponsored by the institution is conducted in compliance with the *Guidelines* and applicable laboratory safety guidance[3–5].

In this case, assuming both institutions have an Animal Welfare Assurance with OLAW, there is no federal requirement for dual IACUC review[1,6]. Agreement between the GEU IBC and the CRO's IBC is the key to resolving the situation. As highlighted in the *Guide for the Care and Use of Laboratory Animals*, "interinstitutional collaborations have the potential to create ambiguities about responsibility for animal care and use"[7]. An expanded written agreement describing IBC and IACUC oversight when disagreements arise would have both institutions well-positioned to quickly resolve the issue. Absent that, the GEU IACUC should make it clear to Dr. Mayfield that work at the CRO may not proceed until the two IBCs agree on necessary safety conditions. ❐

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References

1. Office of Extramural Research, National Institutes of Health. *NIH Grants Policy Statement, Part II, Terms and Conditions of Grant Awards, Part A, Section 4.1.1.3, Consortiums.* (US Department of Health and Human Services, Bethesda, MD, USA, revised December 2019). https://grants.nih.gov/grants/policy/nihgps/html5/section_4/4.1.1_animal_welfare_requirements.htm#Consorti (accessed, November 16, 2020).
2. Office of Extramural Research, National Institutes of Health. *NIH Grants Policy Statement, Part II, Terms and Conditions of Grant Awards, Part B, 15.2.1, Written Agreement.* (US Department of Health and Human Services, Bethesda, MD, USA, revised December 2019) https://grants.nih.gov/grants/policy/nihgps/html5/section_15/15.2_administrative_and_other_requirements.htm#Written (accessed, November 16, 2020).
3. Office of Extramural Research, National Institutes of Health. *NIH Grants Policy Statement, Part II: Part A, Section 4.1.26, Research Involving Recombinant or Synthetic Nucleic Acid Molecules (including Human Gene Transfer Research).* (US Department of Health and Human Services, Bethesda, MD, USA, revised December 2019). https://grants.nih.gov/grants/policy/nihgps/html5/section_4/4.1.26_research_involving_recombinant_or_synthetic_nucleic_acid_molecules__including_human_gene_transfer_research_.htm (accessed, November 16, 2020).
4. Office of Science Policy, National Institutes of Health. *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules.* (US Department of Health and Human Services, Bethesda, MD, USA, revised April 2019) https://osp.od.nih.gov/wp-content/uploads/2019_NIH_Guidelines.htm (accessed November 16, 2020).
5. Office of Science Policy, National Institutes of Health. *FAQs – Interim Laboratory Biosafety Guidance for Research with SARS-CoV-2 and IBC Requirements under the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules.* https://osp.od.nih.gov/biotechnology/interim-lab-biosafety-guidance-for-research-with-sars-cov-2/ (accessed November 16, 2020).
6. National Institutes of Health. *Public Health Service Policy on Humane Care and Use of Laboratory Animals – Frequently Asked Questions. Protocol Review, Question D.8.* (US Department of Health and Human Services, Bethesda, MD, USA, revised 2017) https://olaw.nih.gov/guidance/faqs#621 (accessed November 16, 2020).
7. Institute for Laboratory Animal Research. *Guide for the Care and Use of Laboratory Animals*. 8th edition, p 15, (National Academies Press, Washington, D.C., USA, 2011).