ROPES & GRAY LLP
PRUDENTIAL TOWER
800 BOYLSTON STREET
BOSTON, MA 02199-3600
WWW.ROPESGRAY.COM

MULTI-REGIONAL CLINICAL TRIALS
THE MRCT CENTER of
BRIGHAM AND WOMEN'S HOSPITAL
and HARVARD

July 5, 2023

BY ELECTRONIC SUBMISSION

Re: Request for Information and Comments on the NIH Updated Policy Guidance for Subaward/Consortium Written Agreements

Dear Director James:

This letter is submitted on behalf of Ropes & Gray LLP ("Ropes & Gray") and the Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard ("MRCT Center") in response to the request for information and comments (the "RFI") on the National Institutes of Health ("NIH") Office of Extramural Research Notice to Announce NIH Updated Policy Guidance for Subaward/Consortium Written Agreements (the "Updated Policy Guidance").[1] The Updated Policy Guidance proposes the addition of a new requirement to NIH Grants Policy Statement Section 15.2 pursuant to which the written agreement (*i.e.*, subaward) with the prime awardee of NIH funding must include, "[f]or foreign subrecipients, a provision requiring the foreign subrecipient to provide copies of all lab notebooks, all data, and all documentation that supports the research outcomes as described in the progress report." The Updated Policy Guidance further states that the documentation supporting the research outcomes "must be provided to [the] prime recipient with each scientific update (no less than once every six months) in line with the timelines outlined in the agreement [between the prime recipient and subrecipient]."

Ropes & Gray is a global law firm that advises clients on, among other things, matters involving the receipt and use of federal research grant funding. Ropes & Gray's clients include institutions of higher education, health care systems, and research institutions that conduct significant research activities supported by NIH and other funding sources. MRCT Center is a research and policy center associated with Brigham and Women's Hospital and Harvard University and is dedicated to improving the integrity of multi-regional clinical trials and to promoting best practices regarding biomedical research, particularly research using human subjects or data sourced from human subjects. Ropes & Gray and the MRCT Center (referred to herein as the "undersigned," "us," or "we") have identified sections of the Updated Policy Guidance that we believe warrant revision or clarification. Our specific comments in response to the RFI are set forth below. [2]

[1] 88 FR 36603 (June 5, 2023).
[2] The responsibility for the content of this document rests with its authors, not with the institutions with which its authors are affiliated.

Scope of Documentation

The Updated Policy Guidance requires that foreign subrecipients of NIH funding provide "all lab notebooks, all data, and all documentation that supports the research outcomes as described in the progress report" as part of the documentation that must be provided to, and obtained by, the prime recipient of the NIH funding.

The scope of documentation that the subrecipient must provide to the prime recipient is very broad. The Updated Policy Guidance does not acknowledge that, in many cases, institutions would simply not legally be able to provide **all** data supporting the funded research and that, in other cases, it would be prohibitively impractical for subrecipients to do so. Under the Final NIH Policy for Data Management and Sharing (NOT-OD-21-013), the definition of "scientific data" that prime awardees must make available under a Data Management and Sharing Plan specifically excludes laboratory notebooks, and in response to public comments regarding feasibility concerns, NIH specifically removed language in the draft data management and sharing policy stating that "reasonable efforts will be made to digitize all scientific data."[3] Additionally, in many disciplines, only a subset of data is suitable for cross-border transfer. For example, "all data" may include human health data whose extraterritorial transfer is not permitted by applicable local laws relating to export of such data.

For these reasons, we recommend that NIH consider revising the Updated Policy Guidance to provide greater flexibility to institutions as to the types of documentation that foreign subrecipients may be expected to share with prime awardees. For example, NIH could revise the Updated Policy Guidance to provide that data must be provided at regular intervals, as determined by the prime awardee, to the extent that those data are critical to the prime awardee's ability to document the primary research findings associated with the grant. Such an approach would give discretion to the prime awardee to determine which data are most essential, to determine which data may be permissibly shared or must be altered prior to sharing (for deidentification or anonymization), and to ensure that data are timely provided by the subawardee.

Regular Transfer of Documentation from Subrecipient to Prime Awardee

The Updated Policy Guidance states that supporting materials "must be provided to [the] prime recipient with each scientific update (no less than once every six months) in line with the timelines outlined in the agreement [between the prime recipient and subrecipient]." In our experience, it is uncommon for research collaborators at different institutions to exchange all forms of primary data and documentation on a regular basis, even when the research involves large institutions with significant resources available to assist researchers with data storage and record retention. In light of personnel, technology, or other resource limitations, it may be impossible or infeasible for smaller ex-U.S. subrecipients to provide all documentation to the prime awardee every six months. In addition, it will be similarly impossible or infeasible for many prime awardees to securely host the vast amounts of data the subrecipients will transmit.

[3] See https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-013.html.

We anticipate that this requirement, if implemented in its current form, could deter U.S.-based awardees in marginal cases from seeking collaborators at critical, but small and poorly resourced, foreign entities, which in turn could hinder the optimal design of a scientific study, as well as capacity-building of researchers in low- and middle-income countries.[4] Furthermore, when considering the numerous additional obligations they will take on in collaborating with U.S.-based prime awardees, ex-U.S. researchers may also be deterred from collaborating with prime awardees of NIH funding, to the ultimate detriment of the U.S.-based prime awardees.

Among other concerns, the requirement to regularly transmit all "lab notebooks, all data, and all documentation that supports the research outcomes as described in the progress report" may be viewed as conflicting with the mission of the NIH's Fogarty International Center dedicated to advancing NIH's mission "by supporting and facilitating global health research conducted by U.S. and international investigators, building partnerships between health research institutions in the U.S. and abroad, and training the next generation of scientists to address global health needs."[5]

We think, however, that there may be an alternative that would alleviate some of NIH's data integrity and accountability concerns and policy goals with respect to robust oversight of foreign subrecipients. Specifically, we suggest that NIH consider revising the requirement that foreign subrecipients provide documentation on a quarterly basis, **and instead require that the documentation be retained by the foreign subawardee and made available to the prime awardee or funding entity upon request, and that failure to make supporting materials available in a timely fashion constitutes a material breach of the subaward, which should disqualify that subrecipient from receiving future subawards or other federal research support.** In our view, a clear and express contractual requirement to make supporting materials available in a timely fashion, upon request by the prime awardee or NIH, would more closely align with existing collaborations in all types of research conducted at U.S. institutions, while also establishing a clear expectation that the obligation to make primary data and other records available upon request is an essential element of the subaward, and that failure to abide by this requirement would have lasting consequences for the subawardee's eligibility for future research support.

With such a requirement in place, NIH could evaluate the adequacy of records maintained by foreign subrecipients in a risk-based fashion, working with prime awardees under certain circumstances to ensure that the performance of foreign subrecipients is consistent with the high standards that NIH and prime awardee organizations have established. In reviewing grant applications that outline proposed contributions by foreign collaborators, NIH could also

[4] For example, a recent article published in *Science* focuses on global public health studies involving U.S. awardees that partner with remote sites around the globe. The success of these research partnerships turns on collaborations with sites and researchers that are not associated with large universities with significant resources, and if the Updated Policy Guidance takes effect as written, it could present significant disincentives for U.S.-based prime awardees to partner with these smaller, non-university sites in foreign jurisdictions. See https://www.science.org/content/article/nih-mandate-foreign-partners-u-s-scientists-regularly-submit-all-data-stirs-outcry.

[5] See Fogarty International Center: https://www.fic.nih.gov/About/Pages/mission-vision.aspx.

determine, on a case-specific basis, whether to impose more specific conditions on the foreign collaborator as a condition of its subaward.

In short, we recommend that NIH consider changes to the requirement that supporting materials must be provided to the prime awardee no less frequently than once every six months. We believe that clarification that all specific records retention requirements apply to these research data,[6] in combination with a requirement that the records must be made available promptly upon request of NIH or the prime awardee, would address some of the concerns described in this letter.

Risk-Based Application of Updated Policy Guidance

In the event NIH deems it necessary to proceed with the requirement that subrecipients regularly transmit data to prime awardees, we suggest that NIH consider revising the Updated Policy Guidance to provide that these requirements would apply in a risk-based manner. As detailed above, the broad requirements under the Updated Policy Guidance for all subrecipients to provide substantial documentation to prime awardees on a regular basis will predictably deter some collaborations with smaller and poorly resourced foreign institutions and researchers. As written, the Updated Policy Guidance does not differentiate between types of research activities and the relative risks inherent in each activity; instead, the requirements apply to all subawards involving foreign subrecipients of NIH funding regardless of the subrecipient's field of study and the facilities and equipment used to undertake the work.

An alternative approach would be for NIH to institute these requirements only in regard to research that is more likely to require access to these research records for data integrity and other policy purposes, taking into account the past track record of the subrecipient in regard to data retention, the field of study, the national jurisdiction in which the research by the subrecipient is being conducted, and the necessity that the prime awardee and the funding agency have immediate access to the data and documentation through records held by the prime awardee. For example, research conducted in sanctioned or embargoed countries, research that requires advanced facilities or strict safety regimens (*e.g.*, research taking place in Biosafety Level 3 or 4 laboratories), and research with public safety implications (*e.g.*, dual-use technologies, gain-of-function) could all be subject to the requirement that the prime awardee must be provided primary data and other research records of the subrecipient on a periodic basis. When research does not pose such a risk, the subrecipient should, of course, be expected to make its data and records available upon request of the prime awardee or the funding agency.

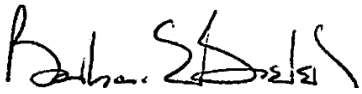
Conclusion

We appreciate the opportunity to provide our thoughts in response to the RFI and to impress upon NIH the challenges we anticipate will be faced by recipients of NIH grant funding if the Updated Policy Guidance is implemented in its current form. We hope and expect that, with the regulated community's collective input and collaboration, NIH can clarify and simplify

[6] See 2 CFR § 200.334; 45 CFR § 75.361; NIH Grants Policy Statement, § 8.4.2 (requiring that recipients of federal funding retain records relevant to the award for three years following the date of submission of the applicable financial report).

expectations for prime awardees and subrecipients of NIH funding to ensure that records of research funded by NIH are secure, accurate, and accessible.

Sincerely,



Mark Barnes, J.D., L.L.M.
Partner, Ropes & Gray
Faculty Co-Director, MRCT Center

Barbara Bierer, M.D.
Professor of Medicine, Harvard Medical School
Faculty Director, MRCT Center