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

January 4, 2024

BY EMAIL

Re: Request for Comments on the Public Health Service Policies on Research Misconduct Notice of Proposed Rulemaking

Dear Ms. Garrity:

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"),[1] as well as the undersigned officials of some the nation's leading academic, research, and research oversight institutions, in response to the notice of proposed rulemaking (the "NPRM") to revise the Public Health Service ("PHS") Policies on Research Misconduct (42 C.F.R. Part 93), issued by the Department of Health and Human Services, Office of Research Integrity ("ORI") on October 6, 2023.[2]

Ropes & Gray is a global law firm that advises clients on research misconduct issues and guides clients through such proceedings, including by performing the functions of acting Research Integrity Officer for research misconduct proceedings. 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, MRCT Center, and officials of the other institutions signing below (collectively referred to herein as the "undersigned," "us," or "we") are supportive of the objectives set forth in the NPRM to align the PHS Policies on Research Misconduct with changes in the research environment since 2005, when the PHS Policies on Research Misconduct were first implemented. To that end, these comments seek to highlight ways that ORI could refine its proposed amendments to ensure clarity and efficiency in implementation for institutions.

[1] The responsibility for the content of this document rests with its authors, and not with the institutions with which MRCT Center is affiliated (Brigham and Women's Hospital, Harvard Medical School, and Harvard University).
[2] 88 Fed. Reg. 69583 (Oct. 6, 2022).

1. Guidance on the Multi-Part Structure of Research Misconduct Proceedings

a. Formalization of Institutional Assessment

In the NPRM, ORI proposes to formalize the institutional assessment phase of research misconduct proceedings by introducing a time requirement at the proposed § 93.306(e) that would require the assessment to be completed within 30 days of initiation. Under the proposed rule, if the assessment takes longer than 30 days to complete, the institution would be required to initiate an inquiry in lieu of completing the assessment.

While we understand the importance of ensuring that institutional assessments are conducted in a timely manner, we believe that a 30-day time limit for the institutional assessment would be excessively rigid. As ORI is aware, the initial scoping of potential research misconduct allegations can be complex. Cases frequently involve multiple respondents, several (if not a dozen or more) published papers or other presentations of work, the need to coordinate with other institutions, and/or complex statute of limitations analyses. Further, a 30-day time period is inconsistent with the traditional complaint intake process at most institutions. Specifically, while some allegations of research misconduct are received by email at a single point in time, other allegations come in through a more traditional "compliance hotline" process, often resulting in a weeks-long process in which an institutional representative engages in a series of conversations with a complainant to gather information gradually. This allows the institution to build trust with a complainant and avoid applying undue pressure on a nervous but willing individual raising concerns in good faith.

For these reasons, a 30-day time limit to complete the assessment would be overly burdensome for institutions. It would lead to rushed assessments that are much more prone to errors in judgment, mistakes in assessing facts, and other undesirable outcomes. Additionally, it would undoubtedly result in procedural unfairness for individuals against whom non-meritorious allegations have been raised, when allegations proceed to inquiry but substantively were suitable for dismissal at the assessment stage. The inquiry process is often a very stressful experience for respondents, and it would be unfortunate to have individuals named as respondents and subject to an inquiry simply because an institution is unable to finish an assessment within 30 days. As an alternate strategy to move institutions to expedite the assessment process, ORI might consider a longer deadline of, for example, 90 days.

b. Deadline at the Inquiry Stage

Currently, if an inquiry lasts longer than 60 days, the institution must simply document the reasons for exceeding the 60-day period in the inquiry report. In the NPRM, ORI proposes that "institutions must notify ORI and request an extension[, and] describe the particular circumstances or issues that would warrant additional time to complete the inquiry."

In our experience, this proposed change is unnecessary and overly burdensome. The majority of inquiries last longer than 60 days. There are many reasons for the extended time period for completion of inquiries, including the need to schedule multiple meetings with inquiry committee members or other finders of fact in order to accommodate their schedules, review evidence, schedule and prepare for interviews (if the finder of fact determines that interviews

should be undertaken), and allow for transcription of interviews, preparation of inquiry reports, and time for respondents to comment on those reports, and the need for Deciding Officials to consider the inquiry reports and associated evidence carefully and reach a final decision. The proposed change, requiring institutions to request extensions from ORI, would add unnecessary administrative burden to an already time-intensive process.[3] Moreover, ORI does not explain in the NPRM how ORI will evaluate institutions' extension requests and the circumstances under which ORI might reject an institution's request for an extension. We believe that the current framework is sufficient, as institutions are held accountable via the requirement to document in writing the reason for exceeding the 60-day period, and ORI has the authority to conduct oversight review, provide guidance to institutions as to their compliance with the PHS Policies on Research Misconduct, and take administrative action if needed. Therefore, we recommend that ORI not proceed with this change in the final rule.

2. Definition of Intentionally, Knowingly, and Recklessly

Since the PHS Policies on Research Misconduct were first issued, the research community has been uncertain about how to apply the standard of recklessness to research misconduct at 42 C.F.R. § 93.104(b). The NPRM attempts to address this confusion by proposing definitions of the three standards that apply to research misconduct: "intentionally," "knowingly," and "recklessly." The proposed definition of "recklessly" is "to act without proper caution despite a known risk for harm."

While we appreciate ORI's attempt to clarify the *mens rea* standards, we believe that the proposed definition of "recklessly" does not provide the level of clarity that is needed in order for the standard to be applied consistently across cases and institutions. As it stands, the proposed definition is both over-inclusive and under-inclusive. For example, one critical issue that often emerges in research misconduct cases is whether a laboratory head or other supervisor should be found reckless on the basis that the supervisor's oversight was deficient and that deficiency led to the falsification, fabrication, or plagiarism at issue. In these cases, applying the definition of "recklessly" used in the NPRM may be problematic. Committees could conclude that the risk of falsification is always a "known risk for harm," and therefore the failure to review all source data for a paper should be deemed "acting without proper caution despite a known risk for harm." This interpretation would result in a very expansive definition of "recklessly," resulting in a low bar for reaching a recklessness finding, and in our view would eliminate any difference between negligence (which is not misconduct) and recklessness. Other committees, however, could emphasize the "known" in the "known risk for harm" standard and conclude that a finding of "recklessly" requires some specific knowledge that the person who falsified, fabricated, or plagiarized research was likely to do so. In those circumstances, it would be virtually impossible to reach a recklessness finding under this narrower interpretation of the proposed definition, and in our view could eliminate any difference between recklessness and knowing or intentional conduct.

[3] ORI's existing practice is to set deadlines at the inquiry stage in cases in which ORI has referred a set of allegations to the institution. We recommend that ORI discontinue this practice as well, so that the approach for deadlines at the inquiry stage does not vary depending on when an allegation is received from ORI or instead from another party.

We acknowledge that it is impossible to define "recklessly" in a fashion that will satisfy all stakeholders and allow for consistent application across all cases. However, we nevertheless think that the definition proposed in the NPRM can be improved. As but one possibility, the undersigned authors from Ropes & Gray and the MRCT Center recently published an article that proposes an alternative, two-part test.[4] In our view, this test would provide for greater consistency in application across cases, and greater precision in the analysis documented in investigation reports. The two-part test is as follows:

> "Part 1: Did the respondent include false, fabricated, or plagiarized data without verifying the accuracy of the information presented?
>
> Part 2: Did the respondent fail to take appropriate and sufficient action to ensure the integrity of the data presented and to mitigate the risk that data were false, fabricated, or plagiarized?"

In addition to refining the proposed definition of "recklessly," we think it is equally important for ORI to publish guidance as to factors that weigh in favor of, and against, a finding of recklessness. Recklessness analyses necessarily turn on the specific facts and circumstances of the specific case at issue, and therefore it would be very helpful, regardless of the exact definition of "recklessly" that ORI chooses to adopt, to lay out examples of fact patterns and/or "plus and minor factors" that would allow an investigation committee to compare and contrast the facts before it with case studies and/or factors that ORI has found to be helpful in past cases. By way of example, in the above-referenced article published by the undersigned authors from Ropes & Gray and the MRCT Center, we outline a series of factors that investigation committees might use to evaluate whether a respondent was reckless.[5] ORI's distribution of guidance to the community detailing how research institutions and ORI itself have appropriately applied the recklessness standard to various research misconduct cases would be immensely valuable.

3. Definition of Honest Error

In the NPRM, ORI proposes to define "honest error" as "a mistake made in good faith," and further to specify that "[a] conclusion of honest error or difference of opinion must not be made at the inquiry stage."

We understand the principle underlying this proposed standard: ensuring that a finding of honest error is made after full review of the evidence. While this is a laudable goal, the standard would likely result in many inefficient and undesirable outcomes. For example, there are thousands of corrigenda, errata, and retractions published each year. Applying the proposed rule, it would appear that nearly every published erratum and corrigendum involving PHS-supported work, if brought to the attention of the relevant institution as an allegation of research misconduct, would require an inquiry and investigation process to adjudicate, even if the mistake in question appears isolated, limited, and readily explainable, with all original data and records available, and was remediated by the authors prior to their knowledge of any research misconduct process being triggered. Such a standard would be unnecessarily burdensome for institutions. Further, as

[4] Caron MM, Dohan SB, Barnes M, Bierer BE. Defining "recklessness" in research misconduct proceedings. Account Res. 2023 Sep 11:1-23. doi: 10.1080/08989621.2023.2256650.
[5] *Id.* (Table 1).

emphasized in our comment regarding the preliminary assessment above, the research misconduct proceeding is often a very stressful experience for respondents, and a rigid standard at the inquiry stage would only exacerbate this stress and perpetuate the perception by many respondents of the severity and procedural unfairness of the research misconduct process.

More generally, there are many cases in which inquiry committees or other finders of fact at the inquiry stage are highly confident that an isolated mistake resulted from honest error, based on a review of the initial evidence available to the fact-finder. We agree that safeguards are needed to ensure that inquiry committees do not readily classify misrepresentations in research as an "honest error" without strong reasons for doing so and would not simply accept such a defense at face value, without substantial corroborating evidence. For example, a common refrain from respondents is that "the issue identified must have been an honest error, because the problem identified is not material to the findings in the paper." It is essential that such a defense not be persuasive proof of "honest error" because, among other factors, the purported "immateriality" of a representation matters nothing to whether the representation was false and constitutes an instance of intentional misconduct. However, we think that a rigid standard at the inquiry stage is not needed to mitigate this problem, and it is extremely important for institutions to have greater discretion in evaluating whether findings of honest error might be warranted at the inquiry stage.

4. Statute of Limitations and Subsequent Use Exception

The subsequent use exception of the PHS Policies on Research Misconduct currently states that "[t]he respondent *continues or renews* any incident of alleged research misconduct that occurred before the six-year limitation through the *citation, republication or other use for the potential benefit* of the respondent of the research record that is alleged to have been fabricated, falsified, or plagiarized." 42 C.F.R. § 93.105(a) (emphasis added). ORI's proposed change to § 93.105(a) would narrow the subsequent use exception such that the exception only applies "when the respondent uses, republishes or cites to the portion(s) of the research record that is alleged to have been fabricated, falsified, or plagiarized." Notably, the proposed change would also require that ORI make the final determination about whether the subsequent use exception applies, given the particular facts of the case.

While we generally agree with the notion that the subsequent use exception in its current form may be unnecessarily broad and not clearly defined, we are concerned that the proposed narrowing of the subsequent use exception may not be operational in practice. The determination of whether a "portion of the research record" has been used, republished, or recited would frequently be challenging for institutions to understand and apply, because citations in a scientific publication do not typically cite to a particular figure or portion of the cited publication. For example, if a 2023 publication cites a 2015 publication, the 2023 publication will generally cite the 2015 publication as a whole, rather that note the specific figure or portion of the 2015 publication being cited. Thus, it would be difficult for institutions—and ORI—to determine whether an allegation is subject to the subsequent use exception under ORI's proposed changes.

Additionally, it may be unnecessarily resource-intensive on the part of ORI, and inefficient for both ORI and institutions, to give ORI the responsibility to review each institution's statute of

limitations analysis in those cases in which the subsequent use analysis leads to a determination that certain allegations fall outside the statute of limitation. In addition to being a resource-intensive responsibility for ORI, the required review of this issue by ORI in each case would slow down the final resolution of cases—leaving many cases pending and institutions uncertain as to their disposition while under ORI review. Critically, there would be many cases in which only a portion of the allegations would be dismissed on statute of limitations grounds, while other allegations against the same respondent would proceed to inquiry. In these situations, the need to wait for ORI's review to approve the dismissal of certain allegations prior to commencing the inquiry process would slow down the fact-finding process.

5. Interview Process

We appreciate the additional guidance outlined in the NPRM pertaining to the interview process. However, we believe that some of the additional requirements would lead to an unduly cumbersome process that will in fact be counter to ORI's objective of streamlining research misconduct proceedings.

As a preliminary matter, the NPRM states that "[a]n institution must interview each respondent, complainant, and any other available person who has been reasonably identified as having information regarding any relevant aspects of the investigation, including witnesses identified by the respondent." For this updated language, which is almost identical to the existing standard under § 93.305(g), we urge ORI to reconsider the reference to "must," by adopting the following language: "[a]n institution must interview each respondent and any other available person who has been reasonably been identified as having information regarding *material* aspects of the investigation *that may be likely to affect to the institution's findings, including complainants and/or witnesses identified by the respondent*." These updates would better align with existing best practice, in which inquiry fact-finders and investigation committees use their discretion to determine the relevant witnesses who should be interviewed. By way of example, many complainants are anonymous and provide complaints via email, with no suggestion that they have any relationship to the researchers who performed the work in question. In this circumstance, many institutions determine that it is not worthwhile to pursue an interview with the complainant, rendering the "must" standard problematic. In other cases in which the laboratory environment becomes a material consideration, one might argue that under the proposed standard, every member of a laboratory during the time in question must be interviewed, even if the evidence to be accrued is predictably duplicative.

We also suggest reconsideration of the provision in the NPRM providing that transcripts of all interviews must be provided to the respondent. Adopting such a practice raises confidentiality concerns and may cause individuals either to refuse to interview with committees or limit their responses for fear of retaliation by a respondent. This is particularly relevant in cases in which a very senior researcher is a respondent, as junior researchers (*e.g.*, current and former laboratory members of the respondent) may believe with some reason that the respondent exerts significant influence over their future career prospects. Respondents are entitled to understand the reasoning in support of an inquiry or investigation committee's determination, but in our view that transparency can often be accomplished by the committee's including interview summaries in its inquiry or investigation report, as opposed to complete copies of transcripts. We also recognize that transcription of interviews may be helpful in ORI's own assessment of cases, and

we suggest that ORI instead consider requiring institutions to generate transcripts of all interviews, and including these transcripts as part of the institutional record, as defined at the proposed § 93.223.

Finally, we recommend that ORI issue guidance clarifying that not all institutional conversations with a respondent during a research misconduct proceeding need to be considered an "interview," to make clear that there are certain conversations that do not need to be recorded or transcribed. For example, discussions between the respondent and a Research Integrity Officer to understand what records may exist supporting the work in question and where such records may be located should not be deemed an "interview" for which a transcript would be required.

6. Multiple Respondents

At the outset of a research misconduct proceeding, institutions typically evaluate which individuals involved in the research in question should serve as respondents. For example, in cases involving published articles, institutions frequently consider which of the first, senior, and/or corresponding authors of the articles in question should be named as respondents, and often conclude that multiple authors (*e.g.*, first and senior/corresponding author) should be named as respondents.

The NPRM proposes that additional emphasis be included in the regulation itself regarding the need for institutions to consider whether specific categories of potential research contributors should be included as respondents in a research misconduct proceeding. As drafted, the NPRM reads, "Notably, the principal investigator, other coauthors on the publication(s), co-investigators on the funding proposal(s), collaborators, and laboratory members who were involved in conducting the experiments that generated the primary data or in generating the text and figures in the research records (e.g., published papers and funding proposals) *must* be considered as potential respondents during the assessment, inquiry, and/or subsequent investigation." (emphasis added).

We generally agree that institutions should evaluate who should be considered a respondent at the outset of a research misconduct proceeding, and throughout the assessment, inquiry, and investigation stages. We also appreciate the principle underlying this proposed additional language: specifically, that allegations may focus on a specific individual, and in practice, institutions may be tempted to include only that individual as a respondent, without considering whether the respondent's co-authors or other collaborators may be directly responsible for the specific images, data, and/or text that is the subject of the allegation(s). In some cases, the failure to identify additional respondents at the outset of a proceeding may result in gaps in the sequestration of relevant records or other problems. However, we think it is problematic for the regulations to list specific categories of research collaborators (laboratory members, co-authors, co-investigators on funding proposals, etc.) and state that institutions "must" consider each such category of individuals as respondents in every research misconduct proceeding. Instead, institutions should carefully examine the facts and circumstances of each allegation and should seek at the earliest possible time to ascertain which co-authors were directly responsible for the images, data and/or text that is the subject of the allegation(s), with the goal of naming as respondents those who most likely bear such direct responsibility. Yet this is not a mathematical

formula readily applied, and institutions should be afforded significant discretion in determining who should serve as a respondent at each stage of the proceeding.

Indeed, flexibility is helpful in expediting and facilitating a research misconduct proceeding, to ensure that institutions are utilizing the time of Research Integrity Officers, committee members, and respondents efficiently. One such example is the situation in which a paper that is the subject of research misconduct allegations has one senior and corresponding author but four or more "co-first authors." In this circumstance, if the paper itself and other readily available information do not make clear which of the co-first authors is responsible for the portions of the paper in question, it may be reasonable to name only the senior author as a respondent and advise the inquiry fact-finder or investigation committee that they may add one or more additional co-authors as respondents as additional information becomes known about who prepared the data, text, or figure in question. This approach avoids the possibility of naming three or more co-first authors as respondents who may have not contributed directly to the portion of the work that is in question.

The NPRM does not expressly prohibit institutions from exercising their discretion in these types of scenarios. However, there are and will continue to be many cases in which, ***with hindsight***, an institution and/or ORI believe that additional or alternative individuals should have been named as respondents at an earlier point in a research misconduct proceeding. If this provision of the NPRM is adopted as written, we think it is likely that many institutions will become very conservative over time with their interpretation of the "must be considered" language, to avoid *ex post* critiques that the institution did not properly evaluate whether an individual should be named as a respondent at the outset of a case, and will begin to err on the side of naming excessive respondents, even if not merited.

For these reasons, we recommend that ORI delete the above-quoted language regarding consideration of respondents and instead, provide guidance on this topic to the research community. In the alternative, we recommend that ORI replace "***must***" with "***may***" and add language at the end of the provision clarifying that institutions are afforded significant discretion in determining who should serve as a respondent.

7. Split Decisions

The NPRM provides that all findings in an investigation report must be unanimous, such that "voting or split decisions by the investigation committee members" are impermissible. While we agree with ORI that unanimous decisions on the part of investigation committees are preferable, we worry about the implications of a rule prohibiting split decisions. As an initial matter, we note that the regulation does not discuss what happens if a unanimous decision cannot be reached. In any event, some cases and some allegations are exceedingly complicated and nuanced, and it is reasonable that individuals may come to different determinations; there should not be a specific deterrent to reaching a split decision. The standard for findings of research misconduct is that the "allegation must be proven by a preponderance of the evidence." Just as preponderance of the evidence is a "more likely true than not" standard (*i.e.*, greater than fifty percent likelihood), we believe that having a majority of the investigation committee vote for a finding of research misconduct should be sufficient to support a finding of research misconduct. Further, at most institutions it is typically a Deciding Official, and not the investigation

committee itself, that reaches official conclusions on behalf of the institution as to whether a respondent committed research misconduct. In our view, it is appropriate to have the Deciding Official make a final decision on the basis of a carefully reasoned investigation report, even if the investigation report provides that the Committee members were split in their final decisions.

Finally, the import of this proposed prohibition on split decisions is that a committee truly deadlocked will remain deadlocked, requiring the entire process to be re-initiated with a new committee until unanimity is reached. This would obviously be extremely inefficient.

8. Publication of Institutional Research Misconduct Findings

For a final administrative action that does not result in a settlement or finding of research misconduct, ORI proposes to implement a new provision at § 93.410(b) that would allow ORI to publish notice of institutional findings and "institutional actions related to the falsified, fabricated, or plagiarized material in the research record, but not the names or other identifying information of the respondent(s)." This proposed mechanism would apply in cases in which ORI determines that "doing so is within the best interests of HHS to protect the health and safety of the public, to promote the integrity of the PHS supported research and research process, or to conserve public funds."

While we appreciate the greater transparency for the published research records that this proposed provision seeks to obtain, we request additional clarifications as to how this mechanism would be utilized. Even if the respondent's name is not used in any publication of findings and institutional actions, the works at issue and other identifying information would likely need to be disclosed to be of any value to the research community. As such, it may be exceedingly difficult simultaneously to (i) publish institutional findings and (ii) protect the anonymity of the respondent against whom no findings of misconduct are made.

Conclusion

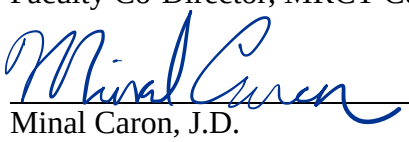
We appreciate the opportunity to provide input in response to the NPRM. We ask that ORI considers our comments when finalizing the revisions to the PHS Policies on Research Misconduct in order to improve the crucial processes surrounding all aspects of research misconduct proceedings and create a more efficient process for institutions charged with reviewing research misconduct, a fairer procedure for respondents, and, ultimately, an even higher reliability of the integrity of research performed with federal funds.

Should you have any questions regarding this letter, do not hesitate to contact the undersigned.

Regards,

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

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



Minal Caron, J.D.
Counsel, Ropes & Gray

/s/ Valerie Bonham
Valerie Bonham, J.D.
Vice President and General Counsel
Kennedy Krieger Institute

/s/ Caren J. Frost
Caren J. Frost, Ph.D., M.P.H.
Associate Vice President for Research Integrity & Compliance
University of Utah

/s/ Susan Garfinkel
Susan Garfinkel, Ph.D.
Consultant
Research Integrity Partners, LLC

/s/ Mark Hurwitz
Mark Hurwitz, Ph.D., P.E.
Chief Research Compliance Officer and Research Integrity Officer
Cornell University

/s/ Mark Lowe
Mark Lowe, M.D., Ph.D.
Vice Chancellor for Research
Washington University in St. Louis

/s/ Giovanni Piedimonte
Giovanni Piedimonte, M.D.
Vice President for Research and Research Integrity Officer
Tulane University

/s/ Kristen Safier
Kristen Safier, J.D., M.S.Ed.
Senior Counsel, Children's National Research Institute
Children's National Hospital

/s/ Elyse I. Summers
Elyse I. Summers, J.D.
President and CEO
Association for the Accreditation of Human Research Protection Programs, Inc. (AAHRPP)

/s/ Ivy R. Tillman
Ivy R. Tillman, Ed.D., C.C.R.C., C.I.P.
Executive Director
Public Responsibility in Medicine and Research (PRIM&R)