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**MULTI-REGIONAL
CLINICAL TRIALS**

THE MRCT CENTER of
BRIGHAM AND WOMEN'S HOSPITAL
and HARVARD

October 31, 2022

BY EMAIL

Re: Request for Information and Comments on the 2005 Public Health Service Policies on Research Misconduct

Dear Dr. Jones:

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 and research institutions,² in response to the request for information and comments (the “RFI”) on the 2005 Public Health Service Policies on Research Misconduct (42 C.F.R. Parts 50 and 93), issued by the Department of Health and Human Services (“HHS”), Office of Research Integrity (“ORI”) on September 1, 2022.³

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 other institutions signing below (collectively referred to herein as the “undersigned,” “us,” or “we”) have identified sections of 42 C.F.R. Part 93 that we believe warrant amendment or supplementation in order to revise, augment, or clarify existing requirements, as described below. Our specific comments and recommendations, offered in response to the RFI, are set forth below.

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 The officials are signing in their personal capacities and not on behalf of the institutions with which they are affiliated, with the exception of Public Responsibility in Medicine and Research, which is signing as an organization.

³ 87 Fed. Reg. 53750 (Sept. 1, 2022).

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

Current Requirements

42 C.F.R. Part 93 requires research misconduct proceedings to follow a multi-part structure, beginning with a threshold review of the allegation and proceeding to an inquiry and an investigation, if warranted. The purpose of the inquiry is “to conduct an initial review of the evidence to determine whether to conduct an investigation,” and the inquiry “does not require a full review of all the evidence related to the allegation[s].”⁴ If the inquiry results in a finding that an investigation is warranted under the standards set forth at 42 C.F.R. § 93.307(d),⁵ the institution must report to ORI the findings of the inquiry and provide the inquiry report.⁶

Suggested Revision, Augmentation, or Clarification

While the regulations provide for an inquiry to be a more preliminary, less exhaustive process than an investigation, we have observed that institutions often convene a committee to conduct a robust, investigation-like process at the inquiry stage, interviewing witnesses and reviewing research records, only to repeat this process at the investigation stage. It would be useful if ORI were to issue guidance that specifies the ways in which institutions have flexibility at the inquiry stage; may, in compliance with the regulations, conduct a more streamlined and simple process at the inquiry stage; and can incorporate findings from the inquiry into the investigation. ***Explicit guidance regarding the steps institutions do not need to take in order to satisfy regulatory obligations at the inquiry and investigation stages would be particularly helpful.*** For example, institutions would benefit from express ORI guidance that they do not need to (1) convene committees of experts to conduct reviews at the inquiry stage to determine whether an investigation is warranted; (2) call witnesses for full recounts of the facts at the inquiry stage, if such recounts are not needed to determine whether the investigation is warranted; or (3) repeat in the investigation stage an interview conducted in the inquiry, unless the investigation committee believes that another interview could reasonably be expected to yield additional material information.

It would also be of enormous practical help if ORI could ***clarify that institutions may close out a proceeding at the inquiry stage if the evidence is straightforward and overwhelming or if honest error explains the data problems.*** In cases in which the institution expects to close out proceedings at the inquiry stage due to a clear finding that there was no research misconduct, such as a finding of honest error, it would be reasonable for ORI to expect institutions to have conducted a robust inquiry, in order to justify the abbreviated proceeding. Finally, it would be useful if ORI could adopt the position, either in regulation or in guidance, that the Research Integrity Officer or another designated institutional official could perform the inquiry, with, if needed, one or more appropriate subject matter experts, without the need for a committee with multiple members. Although the current provisions of Part 93 would appear to allow this, many institutions self-defer from this alternative because it is not cited as an explicit option in Part 93. We believe that such ORI guidance would provide comfort to institutions that

⁴ 42 C.F.R. § 93.307(c).

⁵ 42 C.F.R. § 93.307(d).

⁶ 42 C.F.R. § 93.309(a).

they can conduct a more streamlined process at the inquiry stage in full compliance with the regulations, thereby preserving resources and allowing for more rapid completion of research misconduct proceedings.

2. Definition of Recklessness

Current Requirements

42 C.F.R. Part 93 states that a finding of “research misconduct” requires demonstration by a preponderance of the evidence that falsification, fabrication, or plagiarism was committed *intentionally, knowingly, or recklessly*.⁷ The intentional, knowing, or reckless action must constitute “a significant departure from accepted practices of the relevant research community.”⁸ We have observed through our experience that the “intentionally” and “knowingly” standards are readily understood with reference to the plain meanings of such terms in everyday use. “Intentionally” means that the research was carried out with the respondent’s specific intent to falsify, fabricate, or plagiarize. It equates to the highest level of culpability of the three standards set forth in the regulatory text. “Knowingly” means that the respondent knew the research was falsified, fabricated, or plagiarized. “Knowingly” equates to a lower standard of culpability than “intentionally” because, while it implies the respondent *knew* the research misconduct was carried out, it does not require the respondent to have *intended* the research misconduct to have been carried out. Unlike knowing and intentional conduct, however, reckless conduct cannot be defined with reference to an everyday standard, and “reckless” is not defined under 42 C.F.R. Part 93. Participants in the research misconduct proceeding typically understand the “recklessness” culpability standard to fall below intentional and knowing (both of which constitute research misconduct and are included in its definition) and above honest error and negligence (neither of which constitutes research misconduct, as set forth in the regulatory text).⁹ In our experience, a broad range of conduct often exists between “knowing” conduct and “negligent” conduct in the context of a research misconduct proceeding, and fact-finders and decision-makers struggle to frame and apply an appropriate “recklessness” standard to the respondent conduct they are charged with reviewing.

In our experience, this issue arises most often in research misconduct proceedings concerning respondents who supervised, but did not directly perform, the research at issue. In such instances, the respondent often is, for example, the senior or corresponding author on a publication that uses data found to have been falsified, fabricated, or plagiarized. Evidence in these cases often suggests that the supervising respondent did not know of the problematic data at the time the paper was submitted, but as supervisor, the individual undoubtedly possesses essential responsibility for ensuring the integrity of the research (*e.g.*, if the research at issue was disseminated from the individual’s lab). In the absence of knowing or intentional conduct, the question then becomes whether the failure to ensure the integrity of the research should be construed as “reckless,” such that the respondent should be judged guilty of research misconduct, or mere negligence or honest error, such that the respondent should be judged not to have engaged in research misconduct. The lack of a clear standard or guidance articulated for

⁷ 42 C.F.R. §§ 93.103 and 93.104 (*emphasis added*).

⁸ 42 C.F.R. § 93.104.

⁹ 42 C.F.R. § 93.103.

“recklessness” leads to problematic outcomes, such as time spent seeking to articulate the appropriate standard, and, most alarmingly, inconsistency in outcomes for respondents when, in different proceedings, the individuals charged with judging respondent conduct come to different conclusions regarding the definition of “recklessness” to be applied.

Suggested Revision, Augmentation, or Clarification

For the reasons noted above, we respectfully request further guidance on the standard required for respondent conduct to be determined “reckless.” Within sub-regulatory guidance, for example, ORI could incorporate a definition of “recklessness” and examples of actions that do and do not amount to “recklessness,” giving stakeholders a more detailed and helpful framework by which to assess the conduct with which they are presented. ORI could consider making clear in such guidance that a finding that conduct did not rise to the level of “recklessness” does not preclude a determination that the conduct constituted a violation of professional standards warranting remediation under an institution’s policy.

We believe that these or other changes to the recklessness framework under 42 C.F.R. Part 93 would help to ensure that different fact-finders can reach more consistent decisions under similar fact sets, leading to more efficient and fair outcomes.

3. Confidentiality and Communications with Journals

Current Requirements

42 C.F.R. § 93.108 governs the confidentiality of research misconduct proceedings, limiting the disclosure of “the identity of respondents and complainants” and “records or evidence from which research subjects might be identified” only to those who “***need to know***” such information. Various stakeholders, including institutions, respondents, and their respective counsel have struggled to limit any publicity of the facts surrounding the research misconduct proceeding, in particular the identity of the respondent, and have grappled with defining an appropriate standard for when there is a “need to know.” We have observed this issue in particular when allegations are raised amidst institutional personnel issues, such as respondents being put up for tenure or junior investigators or staff at risk of losing employment; additional compliance concerns at the institution stemming from the alleged misconduct, such as suspensions of grant draw-downs or institutional review board proceedings; and most acutely, questions over the appropriate course of conduct with respect to journal articles that include research that is the subject of an ongoing or completed research misconduct proceeding.

Suggested Revision, Augmentation, or Clarification

ORI would do a great service to the regulated community if, in guidance, ORI would provide examples of circumstances in which there is a legitimate need to inform persons outside of the research misconduct process of aspects of that process, even though the process has not yet concluded. The examples should not be exclusive, but having such examples drawn from common institutional circumstances would assist institutions in dealing with operational challenges. We also believe that it would be helpful for ORI to distinguish more clearly if any confidentiality obligations continue to apply following a finding that there was research misconduct or that there was not research misconduct. We would suggest that if,

following conclusion of the research misconduct proceeding, a respondent is found to have engaged in research misconduct, the priority should become the institution's ability to address the necessary follow-up in response to such a finding. The confidentiality obligation should be relieved such that institutions may address such follow-up through, for example, notification to administration, funders, institutional review boards, prospective employers of the respondent who inquire about past proceedings, journal co-authors and editors, and other entities and individuals without fear of violating the "need to know" standard.

If, on the other hand, the respondent is found not to have engaged in research misconduct, the priority should shift to rehabilitation and protection of the respondent's reputation. The confidentiality obligation in that case should remain, continuing to bind those who are aware of the proceedings from disclosing in the absence of a "need to know" scenario but permitting disclosure when required to clear the respondent's name – as when, for example, a prospective employer inquires about a past proceeding. We recommend that ORI specifically address, in guidance, situations in which a "need to know" requires the disclosure of information relating to a research misconduct proceeding in order to restore a respondent's reputation, and whether the respondent's prior consent must be obtained to make such a disclosure.

4. Statute of Limitations

Current Requirements

42 C.F.R. § 93.105(a) states that 42 C.F.R. Part 93 "applies only to research misconduct occurring within six years of the date HHS or an institution receives an allegation of research misconduct," with certain exceptions. One of these exceptions, which we refer to herein as the "Subsequent Use Exception," provides that the six-year statute of limitations period does not apply to the extent "[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."¹⁰ Moreover, we understand that ORI personnel have opined in recent months that mere inclusion of a paper in a researcher's curriculum vitae or in a grant biographical sketch could constitute a "use for the potential benefit of the respondent" and therefore could trigger the Subsequent Use Exception and, accordingly, re-toll the six-year statute of limitations period. Such an interpretation of the Subsequent Use Exception, if enforced by ORI, would divert critical institutional resources and attention away from more consequential subsequent uses of research, such as citations or republications in seminal, recent papers.

In our experience, the Subsequent Use Exception, as currently written, has created a significant burden for institutions. Institutions often are required to expend time and resources investigating allegations regarding papers that were cited within the last six years but that were themselves published decades ago, and yet to do so requires the expenditure of time and resources that could otherwise be dedicated to investigating allegations regarding more recently published, high-impact papers. Such efforts involve a particularly large expenditure of resources as institutions must seek to explore a body of work authored by individuals who have likely long moved on in their careers and may no longer be focused on the particular subject matter at issue.

¹⁰ 42 C.F.R. § 93.105(b)(1).

We think it is important that institutions be allowed to focus their efforts and resources in the course of a research misconduct proceeding on investigating allegations relating to timelier or more significant uses of research, which have a greater present-day impact on the scientific community.

Suggested Revision, Augmentation, or Clarification

Given the issues described above, ***we request that ORI revoke or amend the Subsequent Use Exception.*** ORI could still encourage institutions, whether by regulation or through guidance, to provide for a longer statute of limitations period under certain circumstances as a matter of institutional policy, such as when a paper published more than six years before the institution received a related allegation of research misconduct is a landmark work in its field and is still frequently cited by other papers, or has formed the basis for patented intellectual property. We support the ability of institutions to use their discretion to review older published research on a case-by-case basis, rather than be required by regulation to review such older research. Further, we recommend that ORI not interpret “use for the potential benefit of the respondent” for purposes of the Subsequent Use Exception as including mere mention of a paper in a researcher’s curriculum vitae or in a grant biographical sketch.

5. Retention of Data

Current Requirements

Neither ORI regulations nor ORI guidance specifies a minimum time period for which institutions must retain data to allow for subsequent confirmation of research findings and to facilitate the sequestration of evidence in the event that a related allegation of research misconduct arises. ORI guidance generally recommends that institutions maintain “a clear retention policy that balances the best interests of society with those of the research institution and the individual researcher,” which may vary depending on the field and the institution.¹¹ As ORI guidance recognizes, different government agencies and programs set forth different requirements regarding the period of retention of data by researchers or institutions.¹² For instance, the National Institutes of Health (“NIH”) Grants Policy Statement generally requires grant recipients to retain all records required by the terms of, or reasonably related to, a grant for a period of three years following the submission of the final financial report to NIH.¹³ NIH’s policy on Data Management and Sharing, set to go into effect on January 25, 2023, encourages researchers to follow longer retention periods than specifically required by NIH policy when factors such as value of the data set to the scientific community and the public warrant such longer retention.¹⁴

¹¹ See ORI, *Data Protection – ORI Introduction to RCR: Chapter 6. Data Management Practices*, <https://ori.hhs.gov/content/Chapter-6-Data-Management-Practices-Data-protection>.

¹² See *id.*

¹³ See NIH, *NIH Grants Policy Statement*, <https://grants.nih.gov/grants/policy/nihgps/nihgps.pdf>, § 8.4.2; see also 2 C.F.R. § 200.334 and 45 C.F.R. § 75.361 (providing for a three-year retention period).

¹⁴ See NIH, *Final NIH Policy for Data Management and Sharing*, NOT-OD-21-013, <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-013.html>.

By contrast, the Food and Drug Administration regulations require sponsors and investigators for Investigational New Drug and Investigational Device Exemption research to retain records for a period of two years from certain points set forth at 21 C.F.R. §§ 312.62 and 812.140, respectively. Meanwhile, under the Privacy Rule issued under the Health Insurance Portability and Accountability Act of 1996 and its implementing regulations, research subjects generally have the right to receive an accounting of certain disclosures of their protected health information made in the six years preceding the request for an accounting, thus requiring study investigators to retain records of disclosures of certain study information for at least six years.¹⁵ It therefore has fallen to institutions to develop their own standards regarding the period of retention of data in compliance with various, divergent regulatory requirements.

Suggested Revision, Augmentation, or Clarification

We recommend that ORI work with federal funding agencies whose research grants are governed by 42 C.F.R. Part 93 to ensure that the various agencies' data retention requirements are compatible. Further, we propose that ORI incorporate into the regulations at 42 C.F.R. Part 93 a requirement for institutions to retain data for a period of at least six years from the date of publication or at least six years from the final financial close-out of the grant that funded the project, whichever is later. This timeline would generally align with the six-year statute of limitations period discussed in Section 4 above. ORI could consider including in guidance the recommendation that, in the case of data relating to a published paper that is a seminal work, institutions should retain such data in perpetuity, and in the case of data that underlie the application for a patent in force, institutions should retain such data for the life of the patent.

6. Subsequent Allegations at Investigation

Current Requirements

42 C.F.R. § 93.310(h) requires institutions to “[p]ursue diligently all significant issues and leads discovered that are determined relevant to the investigation, including any evidence of additional instances of possible research misconduct, and continue the investigation to completion.”

We understand the importance of conducting a robust, timely assessment of any instances of possible research misconduct, including new allegations that arise during the course of an ongoing investigation pertaining to the respondent who is the subject of that investigation. However, in practice, the requirement set forth at 42 C.F.R. § 93.310(h) often makes proceedings unpredictably long and unforeseeably sprawling in scope. While we support ORI’s authority and prerogative to direct evidence of additional instances of possible research misconduct to an institution at any point, including during a proceeding, we believe that institutions would be better able to pursue such leads diligently if they were permitted, but not required, to assess those allegations outside an ongoing investigation and to pursue any additional allegations in a later, separate proceeding or, in consultation with ORI, to use their discretion to resolve the allegations through methods outside the research misconduct process (*e.g.*, seeking retractions or corrections

¹⁵ See 45 C.F.R. § 164.528.

to publications). Relatedly, the rise in online fora for discussing potential data integrity and research integrity issues, such as PubPeer.com, has compounded the problems of an institution being deluged with possible leads, which range widely in terms of significance and credibility, while the institution is trying to conduct a robust investigation regarding pending allegations of research misconduct. The repeated addition of new allegations to ongoing investigations is particularly onerous for smaller institutions with more limited resources.

Suggested Revision, Augmentation, or Clarification

Recognizing ORI's goal of balancing assurance that all allegations of potential research misconduct are adequately examined and assurance that allegations are appropriately resolved in a timely manner, ***we propose that ORI amend 42 C.F.R. § 93.310(h) to make clear that once a proceeding is at the investigation stage, the institution is not obligated to (but may choose to) add to the ongoing investigation new allegations pertaining to the same respondent that come to its attention during the investigation. Further, we would like to reinforce our position that anonymous allegations of data integrity or research integrity issues published on PubPeer.com or other websites should not be considered per se allegations of research misconduct under 42 C.F.R. Part 93 unless they have gone through the institution's process for reviewing allegations and conducting preliminary assessments of those allegations.*** We ask that ORI consider issuing guidance to make this point clear and definitive.

7. Time Limits

Current Requirements

42 C.F.R. Part 93 requires an institution to “complete the inquiry within 60 calendar days of its initiation unless circumstances clearly warrant a longer period,” in which case “the inquiry record must include documentation of the reasons for exceeding the 60-day period”¹⁶ and to “complete all aspects of an investigation within 120 days of beginning it, including conducting the investigation, preparing the report findings, providing the draft report for comment . . . and sending the final report to ORI.”¹⁷

Suggested Revision, Augmentation, or Clarification

In our experience, these time limits are exceedingly difficult to meet (even when institutions are presented with relatively uncomplicated fact sets or “simple” cases, and particularly when additional allegations are added throughout the proceeding), requests for extensions (borne out of necessity) are common, and the possibility of seeing an inquiry or investigation through to a thorough completion in the required timeframes is remote. ***We therefore recommend that the regulatory timeframes be doubled to permit 120 days for completion of the inquiry and 240 days for completion of the investigation.*** Many proceedings would still necessitate requests for extensions due to the sheer volume of issues that must be chased down. However, we expect such requests would become less frequent and more

¹⁶ 42 C.F.R. § 93.307(g).

¹⁷ 42 C.F.R. § 93.3111(a).

institutions would find it possible to complete the inquiry and investigation within the stated time limits, thereby reducing the administrative burden both on ORI and on institutions.

8. Reporting to Federal Funding Agencies

Current Requirements

NIH has stated that an institution's "engagement with ORI as provided in 42 CFR Part 93 does not substitute for its engagement with NIH to ensure ongoing compliance with the terms and conditions of [an] award."¹⁸ 42 C.F.R. Part 93 does not specifically address when and how institutions or respondents should report the status of ongoing proceedings or the results of such proceedings to NIH or other federal agencies that fund research falling under ORI's jurisdiction. Further, 42 C.F.R. Part 93 also does not specifically address if this reporting is consistent with the strict confidentiality requirements in 42 C.F.R. § 93.108.

Suggested Revision, Augmentation, or Clarification

It would be helpful if ORI could work with NIH and other federal funding agencies, including agencies that fund research not directly subject to 42 C.F.R. Part 93, such as the Department of Defense and the Department of Energy, to determine an appropriate standard for what should be reported to federal funding agencies regarding research misconduct proceedings, when those reports should be made, and whether these agencies meet the "need to know" criteria in 42 C.F.R. § 93.108.

9. Appeals

Current Requirements

42 C.F.R. Part 93, Subpart E governs appeals to administrative law judges in the event that findings of research misconduct are made by ORI. 42 C.F.R. § 93.519 applies the Federal Rules of Evidence to certain aspects of the appeals hearing process, such as admissibility standards for character evidence, and the inadmissibility of evidence about offers of compromise or settlement made in the action. Further, 42 C.F.R. § 93.519(b) allows administrative law judges to apply the Federal Rules of Evidence more broadly "where appropriate" (such as "to exclude unreliable evidence").

The appeals process, as set forth at 42 C.F.R. Part 93, Subpart E, is reportedly laborious in terms of time and resources for ORI staff, which is disadvantageous to the regulated community, and which can be demoralizing to institutions, especially after conducting long, thorough, and fair research misconduct proceedings. Moreover, the appeals process applies standards that were not required to be used in the original research misconduct proceeding, such as the evidentiary standards described above.

¹⁸ See NIH, *Responsibilities of Recipient Institutions in Communicating Research Misconduct to the NIH*, Notice Number: NOT-OD-19-020 (Oct, 17, 2018), <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-19-020.html>.

Suggested Revision, Augmentation, or Clarification

We encourage ORI to consider amending the appeals process to allow for more expedient resolutions in general, or at least under certain circumstances. We defer to ORI to determine whether this would warrant amending the evidentiary standards articulated in 42 C.F.R. § 93.519 and/or amending other regulations set forth in 42 C.F.R. Part 93, Subpart E.

Conclusion

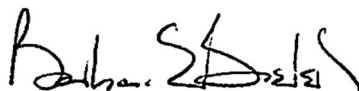
Ropes & Gray, MRCT Center, Public Responsibility in Medicine and Research, and the undersigned officials greatly appreciate the opportunity to provide input on the foregoing in response to the RFI and to impress upon ORI the challenges faced by well-intended stakeholders in conducting research misconduct proceedings. We hope and expect that, with the regulated community's collective input and collaboration, ORI can improve the crucial processes surrounding all aspects of research misconduct proceedings and create a better 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.

Sincerely,



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