

November 12, 2018

Dear Drs. Tabak and Lauer,

The undersigned organizations appreciate the opportunity to comment on the NIH [Registration and Results Reporting Standards for Prospective Basic Science Studies Involving Human Participants](#) (NOT-OD-18-217) through the request for information (RFI) published on August 10, 2018. In this response, our organizations will focus on promoting the following two objectives:

- Maintaining the distinction between basic science and clinical trials while increasing transparency and reporting for basic science studies involving human participants; and,
- Fostering the development of efficient and effective processes and frameworks for the treatment and reporting of basic science research

In providing these comments, we would like to stress that we do not accept the premise of the RFI that basic research studies involving human participants are clinical trials. Each is recognized across all science as a distinct sphere, involving its own design, terminologies, and publication outlets, and, importantly, would involve different practices for registration and reporting. We would therefore oppose NIH funding announcements that do not accept and enforce this distinction (for example as recently proposed in [NOT-OD-19-024](#)).

Maintaining the Distinction Between Basic Science and Clinical Trials While Increasing Reporting for Basic Science

In mid- to late-2017, many from the research community, including [associations](#), organizations, and [societies](#) representing research institutions, medical centers, and scientists (as well as [scientists](#) and institutions individually), expressed concern that NIH had, practically speaking, broadened its definition of “clinical trial” through [revisions to its case studies](#), expanding the scope to include a number of areas of basic science research involving human participants. The new and revised case studies vary substantially from previous cases published [at the time of](#), and subsequent to ([April 2015](#) and [September 2016](#)), the October 2014 publication of NIH’s revised definition of “clinical trial”, greatly expanding the interpretation of an “intervention”¹ and **retroactively subjecting these studies to agency policies specific to clinical trials as well as any future policies and requirements.**

¹ NIH defines an intervention as “a manipulation of the subject or subject’s environment for the purpose of modifying one or more health-related biomedical or behavioral processes and/or endpoints. Examples include: drugs/small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and, diagnostic strategies.”

We affirm, as many of our organizations have previously, that “prospective basic science studies involving human participants” are not clinical trials - nor are they “trials” generally. This research does not fit the 2014 definition as confirmed by the 2014 case studies, and should not be subject to NIH policies, forms, and requirements specific to clinical trials. We believe that designating as “clinical trials” a category of basic research involving human participants is factually invalid and confusing for the research community, agency staff, and the public. The four questions that NIH has put forward to guide the research community in making this determination are very broad and encompass a great deal of basic research. This is not consistent with the designations made in the case studies or by agency staff, resulting in an inefficient and inconsistent process. This particular change of including basic science in clinical trials represents a significant departure from past practice and, to our knowledge, was not subject to extensive consideration involving dialogue and collaboration with the research community at the outset. Such an approach is corrosive to the historical partnership between NIH and its stakeholders.

Recommendations

- We strongly recommend that NIH not adopt the proposed designation of “prospective basic science studies involving human participants”, and simply require reporting of all NIH-funded basic science studies involving human participants in a manner that both: (a) avoids subjecting these studies to clinical trial requirements and (b) is developed in consultation with stakeholders. We believe this would address NIH’s concerns about providing greater transparency, while minimizing confusion and administrative work.
 - NIH should immediately delay publication of new parent funding opportunities that refer to this designation (as announced in NOT-OD-19-024 on October 26, 2018); and,
 - NIH should revise the current clinical trial case studies to be consistent with previous iterations published at the time of the agency’s revised definition of “clinical trial” (October 2014) which did not include basic science research.

Developing Efficient and Effective Processes for Reporting Basic Science

Reporting clinical trials in the ClinicalTrials.gov database is expected to take, per federal estimates, an average of 40 hours per study, and includes strict reporting formats, requirements, and windows for completion. For basic science research, clinical trials reporting formats are often not compatible with how research is conducted and reported. Further, basic science moves at a fast pace and can take many forms for which 40 hours per study of reporting requirements may be a significant underestimation. For example, some basic research domains involve running many studies over the course of a few weeks or months, launching new experiments on a weekly basis, and adjusting approaches or study parameters based on “trial and error” phases. Moreover, in many contexts, this work is accomplished by a small team or single individual. The ClinicalTrials.gov platform does not easily lend itself to reporting basic science research where the parameters are frequently adjusted, and it contains many variables that are irrelevant in these basic research contexts. Variables such as clinical end points, conditions, arms and interventions, and outcome measures are geared toward

clinical research and how that research is regulated, not basic science, which will have significant variance in its design, goals, and structure.

Registration and reporting standards that are not well suited to studies not involving patient visits, data safety monitoring, or treatment options are inefficient and ineffective, and regulatory requirements that are unnecessary should not divert limited resources in this way. The requirements will tax researchers and the administrators assisting them and would seem to be of limited benefit to researchers or patients (indeed, many if not most basic research studies do not involve patients at all). The burden will be particularly heavy for small and mid-size research programs with fewer financial resources and will be compounded by the need to replicate the same reporting procedures for many smaller studies—multiplying the effort per award many times over for some basic researchers. Institutions with substantial resources have hired numerous individuals to assist with entering this information for clinical trials, but for many institutions this is not possible and may lead to inadvertent noncompliance or could force investigators at these institutions to choose another research path.

Finally, besides reporting compliance, a purpose of registration is to improve the rigor and reproducibility of the reported research. A process that is bureaucratically burdensome may prevent researchers from personally registering their projects and benefiting from the planning process for their research rigor. An effective registration system for basic research would be sensitive to the realities of doing this research and efficient enough to be integrated into the researchers' workflow.

Recommendations

Reporting basic science research through use of existing data collections, including grant applications and progress reports, and/or through alternative portals and frameworks for managing experiments and workflow that can interface with federal databases, could reduce unnecessary administrative work on the part of investigators and institutions, and would also make the end result useful to basic and clinical researchers.

- NIH should appoint a working group of the Advisory Committee to the Director and identify other means for working collectively with the community to establish appropriate standards and frameworks for reporting all basic science studies involving human participants and to determine where that information should be stored. These efforts should include the following:
 - Consider what basic information is needed to appropriately inform the research community of previous and ongoing work in non-clinical basic research.
 - Strongly consider how existing data collection methods and IT resources can be utilized in support of this effort, including the use of RePORTER, summary information on grant applications, and searchable key words. It could involve release of “in progress” and final grant reports, or aspects of them, without Freedom of Information Act requests.

- Make use of the Open Science Framework (<http://osf.io/>) and/or other frameworks available now and in the future, for reporting all basic science studies involving human participants by enabling those frameworks to interface with federal databases such as ClinicalTrials.gov in an area separately designated for basic research. In this respect, NIH should consider renaming ClinicalTrials.gov or, at least, clearly labeling a basic science area within that database.
- Allow working group recommendations to be vetted by the community through a request for public comment.

We appreciate the opportunity to comment on this RFI and look forward to working with you to identify a mutually agreeable path forward. Responses to the RFI questions, which include parts of this letter, can be found below. Organizations listed on this letter may submit separate responses to the RFI questions. If you have questions about the content of this letter, or for follow-up, please contact Lisa Nichols, Ph.D., Director for Research and Regulatory Reform at the Council on Governmental Relations at lnichols@cogr.edu or 202-289-6655.

American Anthropological Association

American Association for the Advancement of Science

American Educational Research Association

American Psychological Association

American Society for Investigative Pathology

American Sociological Association

Association for Psychological Science

Association for Research in Vision and Ophthalmology

Behavior Genetics Association

Consortium of Social Science Associations

Council on Governmental Relations*

Federation of Associations in Behavioral and Brain Sciences

The International Society for Developmental Psychobiology

Linguistic Society of America

Population Association of America and Association of Population Centers

Psychonomic Society

Society of Multivariate Experimental Psychology

Society for Personality and Social Psychology

The Society for Prevention Research

Society for Psychophysiological Research

Society for Research in Child Development

The Society for Social Work and Research

Vision Science Society

*Although COGR represents 187-member institutions, the following institutions requested that we also note their strong endorsement of this letter by signing on individually:

Boston University

Brown University

Duke University

Florida State University

Harvard University

Indiana University

Michigan State University

New York University

Partners HealthCare

Princeton University

Purdue University

Stanford University

University of Alabama

University of Alabama at Birmingham

University of California

University of Iowa

University of Kansas

University of Michigan

University of Rochester

University of Washington

University of Wisconsin-Madison

Washington University in St. Louis

Yale University

RFI questions: The NIH seeks comments on any of the following topics:

- Specific examples of prospective basic science studies involving human participants that pose the greatest challenges in meeting the registration and results information submission requirements at ClinicalTrials.gov, including specific reasons for these challenges (e.g., specific data elements);
 - Reporting clinical trials in the ClinicalTrials.gov database is expected to take, per federal estimates, an average of 40 hours per study, and includes strict reporting formats, requirements, and windows for completion. For basic science research, clinical trials reporting formats are often not compatible with how research is conducted and reported. Further, basic science moves at a fast pace and can take many forms. For example, some domains involve running many studies over the course of weeks or months and adjusting approaches or parameters based on "trial and error" phases. The ClinicalTrials.gov platform does not easily lend itself to reporting basic science research under these circumstances, and it contains many variables that are irrelevant in these basic research contexts. Variables such as clinical end points, conditions, arms and interventions, and outcome measures are geared toward clinical research and how that research is regulated, not basic science, which will have significant variance in its design, goals, and structure.
 - We understand from researchers that discovery or observational studies and pilot studies with low numbers of human participants would present significant challenges in meeting the registration and results information requirements in ClinicalTrials.gov. Discovery and observational studies do not simply test a particular binary hypothesis. Consider a set of pilot studies or basic science studies that might consist of 10 small studies with 10 subjects each. The data entry demands would be ten times greater than on one large study with 100 subjects. Exploratory research, basic behavioral research, cognitive and brain research and benign behavioral interventions would all reportedly be negatively impacted. Research without specific applications to products and processes is unlikely to fit well with current reporting requirements. Studies that involve the use of graphs and images (e.g., fMRI studies) would also not fit well with the current platform which uses data tables. More options for reporting data would be needed. Further, clinical trial statistical considerations may not apply to exploratory or pilot studies.

- **Strengths and weaknesses of potential alternative platforms that might function as conduits for timely registration and reporting of prospective basic science studies involving human participants;**

Reporting basic science research through use of existing data collections, including grant applications and progress reports, and/or through alternative portals and frameworks for managing experiments and workflow that can interface with federal databases, could reduce unnecessary administrative work on the part of investigators and institutions and would also make the end result useful to basic and clinical researchers.

- NIH should appoint a working group of the Advisory Committee to the Director and identify other means for working collectively with the community to establish appropriate standards and frameworks for reporting all basic science studies involving human participants and to determine where that information should be stored. These efforts should include the following:
 - Consider what basic information is needed to appropriately inform the research community of previous and ongoing work in non-clinical basic research.
 - Strongly consider how existing data collection methods and IT resources can be utilized in support of this effort, including the use of RePORTER, summary information on grant applications, and searchable key words. It could involve release of “in progress” and final grant reports or aspects of them without Freedom of Information Act requests.
 - Make use of the Open Science Framework (<http://osf.io/>) and/or other frameworks available now and in the future, for reporting all basic science studies involving human participants by enabling those frameworks to interface with federal databases such as Clinicaltrials.gov in an area separately designated for basic research. In this respect NIH should consider renaming Clinicaltrials.gov or, at least, clearly labeling a basic science area within that database.
 - Allow working group recommendations to be vetted by the community through a request for public comment.
- **Additional data elements or modification to existing data elements that could be applied to ClinicalTrials.gov to better meet the needs of the public and of researchers in assuring timely registration and results information submission of prospective basic science studies involving human participants;**
 - ClinicalTrials.gov was designed to be a source of public information as well as a tool for individuals to see which studies are appropriate or available for them to participate in as a clinical trial subject. It will be confusing to repurpose ClinicalTrials.gov for reporting of early stage basic research that may take decades to be relevant to the

public. In addition, the influx of new studies may dilute NIH oversight and monitoring of true clinical trials.

- **Other existing reporting standards for prospective basic science studies involving human participants and how such standards would fulfill the aims described in the NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information.**
 - We believe it would serve no useful purpose to answer this question in the context of this RFI, which, as we have stressed previously, inaccurately classifies basic research that includes human subjects as clinical trials.
- **Any other point the respondent feels is relevant for NIH to consider in implementing this policy for timely registration and reporting of prospective basic science studies involving human participants.**
 - In mid- to late-2017, many from the research community, including [associations](#), organizations, and [societies](#) representing research institutions, medical centers, and scientists (as well as [scientists](#) and institutions individually), expressed concern that NIH had, practically speaking, broadened its definition of “clinical trial” through [revisions to its case studies](#); expanding the scope to include a number of areas of basic science research involving human participants. The new and revised case studies vary substantially from previous cases published [at the time of](#), and subsequent to ([April 2015](#) and [September 2016](#)), the October 2014 publication of NIH’s revised definition of “clinical trial,” greatly expanding the interpretation of an “intervention” and **retroactively subjecting these studies to agency policies specific to clinical trials as well as any future policies and requirements.**
 - We affirm, as many of our organizations have previously, that “prospective basic science studies involving human participants” are not clinical trials - nor are they “trials” generally. This research does not fit the 2014 definition as confirmed by the 2014 case studies, and should not be subject to NIH policies, forms, and requirements specific to clinical trials. We believe that designating as “clinical trials” a category of basic research involving human participants is factually invalid and confusing for the research community, agency staff, and the public. The four questions that NIH has put forward to guide the research community in making this determination are very broad and encompass a great deal of basic research. This is not consistent with the designations made in the case studies or by agency staff, resulting in an inefficient and inconsistent process. This particular change of including basic science in clinical trials represents a significant departure from past practice and, to our knowledge, was not subject to extensive consideration involving dialogue and collaboration with the research community at the outset. Such an approach is corrosive to the historical partnership between NIH and its stakeholders.

Recommendations

- We strongly recommend that NIH not adopt the proposed designation of “prospective basic science studies involving human participants”, and simply require reporting of all NIH-funded basic science studies involving human participants in a manner that both: (a) avoids subjecting these studies to clinical trial requirements and (b) is developed in consultation with stakeholders. We believe this would address NIH’s concerns about providing greater transparency, while minimizing confusion and administrative work.
 - NIH should immediately delay publication of new parent funding opportunities that refer to this designation (as announced in NOT-OD-19-024 on October 26, 2018); and,
 - NIH should revise the current clinical trial case studies to be consistent with previous iterations published at the time of the agency’s revised definition of “clinical trial” (October 2014) which did not include basic science research.