FASEB
Federation of American Societies for Experimental Biology

Representing Over 130,000 Researchers

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Comments submitted via email to: francis.collins@nih.gov, lawrence.tabak@nih.gov, and michael.lauer@nih.gov , and electronically at: https://grants.nih.gov/grants/rfi/rfi.cfm?ID=80

Dear Drs. Collins, Tabak, and Lauer:

The Federation of American Societies for Experimental Biology (FASEB) appreciates the opportunity to respond to the Request for Information (RFI): Registration and Results Reporting Standards for Prospective Basic Science Studies Involving Human Participants (NOT-OD-18-217). Comprising 30 member societies which collectively represent 130,000 basic, clinical, and translational researchers, FASEB respects the importance of transparency and accountability in publicly-funded research. We commend the National Institutes of Health (NIH) for recognizing and seeking to address the under-reporting of results from NIH-supported clinical trials through policy and consultation with the regulated community. Our concern, and one shared by many basic biomedical researchers, is the requirement in the NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information that all studies meeting the NIH definition of "clinical trial" must be registered and have summary results reported in clinicaltrials.gov. This requirement is not well-suited to the expanding scope of research conducted with human participants that is considered to be a clinical trial by NIH.

Through its updated definition of "clinical trial" and the interpretation of that definition as exemplified by the addition and refinement of case studies on its clinical trials web page, NIH has effectively created three categories of human subjects research. First, there are studies that meet the definition of "applicable clinical trial" from the Food and Drug Administration Amendments Act (FDAAA) of 2007 as well as the NIH definition of "clinical trial." These studies must be registered and summary results reported in clinicaltrials.gov, as required by FDAAA. Applicable clinical trials are studies that compare the effect of an intervention (i.e., a device, drug, or biologic product) versus control on a health outcome.

Second, there is human subjects research that meets the NIH definition of "clinical trial," but not the FDAAA definition of "applicable clinical trial." According to NIH policy, these studies must also be registered and the results reported in clinicaltrials.gov, despite the fact that many of them do not constitute the type of research generally thought of as clinical trials. Third, there are studies involving humans that do not qualify as either applicable clinical trials or NIH-defined clinical trials; there are currently no registration and reporting requirements for this research. Unfortunately, delineating the differences between these two categories is often difficult, creating confusion for researchers and NIH staff alike as to which studies must comply with NIH's Dissemination Policy.

The focus of this RFI, and of much consternation in the basic research community, is the second category—basic, or fundamental, research involving human participants that, because of NIH's expansive interpretations of "intervention" and "health-related biomedical or behavioral outcomes," are now considered clinical trials. FASEB agrees that clinical trials should be posted in a publicly-available and searchable repository, and that this benefits both the research community and the public. However, the Federation believes that basic research, regardless of whether it meets the NIH definition of "clinical trial," should not be included in the clinicaltrials.gov system. Clinicaltrials.gov is not optimized for these types of studies, which often don't fit the traditional two-arm comparator design or produce quantifiable endpoints or outcomes. Moreover, the public at large is not looking for basic research studies if and when they access clinicaltrials.gov.

FASEB understands NIH's position: that the sacrifice and altruism of human research participants should be recognized through publication of the research in a public database. We do not understand, however, why that recognition should be extended to some participants and not others based solely on NIH's interpretation of its definition of "clinical trial," especially when the differences between the studies in which they participate can be negligible. FASEB recommends, therefore, that NIH require all research studies involving human participants to be registered and summary results reported in a public, searchable database. This policy change would ease the confusion for researchers created by NIH's updated definition of "clinical trial," and more equitably respect all research volunteers. Furthermore, we suggest that clinicaltrials.gov should only be used as a registration and reporting platform for those studies for which it was created: applicable clinical trials. Our suggestion for an alternative to clinicaltrials.gov for a registration and reporting platform for basic research studies is detailed below.

Topic #2: "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."

FASEB proposes that NIH use its Research Portfolio Online Reporting Tools Expenditures and Results (RePORTER) system as an alternative to the clinicaltrials.gov database to facilitate research reporting requirements for all studies it funds involving human participants that **do not** meet the criteria outlined in FDAAA for applicable clinical trials. NIH-funded clinical studies that **do** qualify as applicable clinical trials should be expected to meet all registration and reporting requirements mandated through 42 CFR Part 11 (i.e., the "Final Rule," which clarifies reporting requirements in FDAAA Section 801).

One of the primary drivers of the NIH Dissemination Policy is responsible stewardship of taxpayer funds. Mandating clinical trials to be registered and to report results in a public database like clinicaltrials.gov allows other researchers to see what studies have already been done and those being conducted. This should minimize duplication of effort and reduce waste. Furthermore, when it is providing the funds, the public should be able to identify clinical trials that are currently recruiting and obtain summary results from those that have concluded. FASEB agrees with both of these premises. However, for the many exploratory, mechanistic, observational, and other types of basic research studies now classified as clinical trials, the most useful information—for both other researchers and the public—about a given study would be a short summary of the purpose, hypotheses tested, and basic findings.

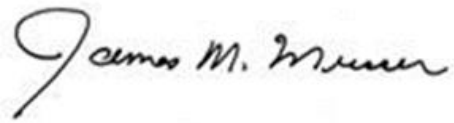
RePORTER is a searchable, public database maintained by NIH that is continually updated with all current NIH grant awards. For each grant the system displays a project description, key terms, award amount and history, project start and end dates, and any resulting publications and patents, among other information. Recently, NIH updated its policies such that Project Outcomes—concise, lay-language summaries of research findings taken directly from principal investigators' (PIs') interim or final Research Performance Progress Reports—will be included in RePORTER. As the number of grants for which outcomes are available increases so, too, will RePORTER's utility as a registration and reporting platform. Additionally, RePORTER provides contact information for the PI, so that interested parties could ask for more detailed information or data, should they choose.

Adding a few search features to the existing RePORTER database would enhance the retrieval of information about basic research that involves human participants. For example, now that all grants proposing clinical trials must be submitted through specific Funding Opportunity Announcements (FOAs), there should be a way in the RePORTER query form to refine a search by FOA type (i.e., clinical trial allowed, optional, or not allowed). In addition, or alternatively, since all grants involving research with human participants must submit a Human Subjects and Clinical Trials Information form, there could be a check box in the query form to only search awards with a corresponding Human Subjects form.

Although not created as a research registration and reporting platform, using RePORTER in this manner could confer a number of advantages for NIH, researchers, and the public.

FASEB appreciates NIH's commitment to transparency and accountability to the public and to research volunteers. We think our proposed solution for the registration and reporting of results of all human subjects research is a reasonable compromise that meets all regulatory requirements, while also respecting the contributions of all research participants. If you have any questions, do not hesitate to contact me.

Sincerely,



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