June 6, 2017

Francis Collins, M.D., Ph.D.
Director, National Institutes of Health
9000 Rockville Pike, Building 1
Bethesda, MD 20892

Re: Clarification of NIH Clinical Trial Policy

Dear Dr. Collins:

The Association for Psychological Science (APS) urges NIH to issue a clarification of the NIH Clinical Trial Policy. Specifically, the NIH definition of an “intervention” within the NIH definition of a clinical trial (NOT-OD-15-015) is exceptionally broad and appears to encompass any manipulation of a variable hypothesized to have an impact on a measured behavioral outcome. The broadening of the definition of a clinical trial coupled with the requirement that applications be submitted under a clinical trial-specific funding opportunity announcement (FOA; NOT-OD-16-147) will certainly have a negative impact on basic behavioral science.

The undue burden placed on researchers, institutions, and NIH in terms of the application process, conduct of research, and monitoring requirements is enormous. This broad interpretation is not in keeping with the spirit of the definition of an intervention in the context of a clinical trial. Clarification of the definition of an “intervention” would go a long way in helping the community understand how to submit basic behavioral science applications for NIH funding and would ease the monitoring burden that is certain to overwhelm researchers, institutions, and NIH staff should this broad definition remain.

With the broad interpretation of an “intervention” encompassing any manipulation of a variable hypothesized to have an impact on a measured behavioral outcome, a huge number of applicants will be impacted by this policy change. For those Principal Investigators who are able to submit an application successfully, their applications may be disadvantaged in review because so many of the requirements of a true clinical trial (e.g., a treatment study) will not apply to their applications. Reviewers will clearly be overburdened with additional application materials, review guidelines, and may become frustrated with the application format, number of sections deemed not applicable, and may even have difficulty distinguishing true clinical trials from quasi clinical trials captured with the new definition.

By way of example, a simple review in RePorter found a sampling of research projects that appear to fit the new NIH definition of a clinical trial, but clearly are not a clinical trial. Given their research aims, these types of behavioral studies should not be subjected to the application and reporting/monitoring requirements of clinical trials.
• R01MH090786; PI: Joan Luby and Deanna Barch; Neuroimaging in Early Onset Depression: Longitudinal Assessment of Brain Changes. This award, currently in its 8th year of funding, was submitted for funding via the Parent R01 FOA and is not currently coded as a clinical trial. Under the new definition, this clinical research project would be coded as a clinical trial as the study examines the effect of “interventions”, namely imaging studies, hormonal, and psychosocial assessments, on neural circuitry and developmental trajectories.

• R01AG008441; PI: Daniel Schacter; Aging Memory. This award, currently in its 25th year of funding, was submitted for funding via the Parent R01 FOA and is not currently coded as a clinical trial. Under the new definition, this clinical research project would be coded as a clinical trial as it proposes a series of experiments manipulating cognitive processes involved in memory to distinguish between specific age-related changes in memory versus more general changes in motivation or attention.

• R01DC000491; PI: Susan Goldin-Meadow; From Spontaneous Sign Systems to Sign Language. This award, currently in its 28th year of funding, was submitted for funding via the Parent R01 FOA and is not currently coded as a clinical trial. Under the new definition, this clinical research project would be coded as a clinical trial as the study examines the manipulations of 3 central aspects of sentence structure (verb structure, argument-specification, and sentence-modulation) across a three generations of signers in Nicaragua.

Time is of the essence in considering a clarification to the definition of an “intervention.” Researchers need time to prepare. NOT-OD-17-043 notes that effective January 25, 2018, “all applications involving one or more clinical trials be submitted through a Funding Opportunity Announcement (FOA) specifically designed for clinical trials…. After that date, applications planning a clinical trial that are submitted to a non-clinical trial FOA will be returned without review.” This is particularly problematic. At a minimum, NIH should consider delaying the effective date of this policy until the definition of what constitutes an intervention can be adequately clarified. But we hope that the clarification of the term “intervention” could be quickly accomplished so that such a delay could be avoided.

In reviewing some of the requirements outlined in FOAs already published related to clinical trials, they do not appear to relevant to many basic behavioral studies. As guidance, in May of this year, you noted that the Food and Drug Administration template for clinical trials may be a useful tool for NIH clinical trial applicants. This seems unlikely for basic behavioral manipulations studies such as those cited above. It poses an excessive workload on the part of each Institute and Center to publish clinical trial-specific FOAs to fit each type of intervention (therapeutic vs. non-therapeutic; basic vs applied; patient sample vs healthy control) and for each activity code (e.g., Research Project Grants, Career Development Awards, Fellowship Awards to name a few) and an excessive burden on applicants to wade through this large number of FOAs.

As an organization that has been a leader in the field in emphasizing scientific rigor, registration of research protocols, and research reproducibility, APS fully supports NIH’s effort to enhance the management and oversight of clinical trials and the goal to accelerate the discovery of beneficial interventions for patients in need. But we strongly urge NIH to examine clinical research carefully, that is research involving human subjects, and to be cautious of
implementing an overly inclusive definition of an intervention in the case of a clinical trial. Not all manipulation(s) of controlled variable(s) hypothesized to have an impact on a measured behavioral outcome should be considered together. It is our opinion that every intervention does not make a clinical trial.

Thank you again for your leadership and stewardship in the area of clinical trials research. APS recognizes that NIH is the largest public funder of clinical trial research in the United States. We hope that the issues outlined above will encourage a clarification to the extraordinarily broad definition of “interventions” in the NIH definition of clinical trials. I would be pleased to discuss these issues with you further and welcome your response.

Sincerely,

Sarah Brookhart  
Executive Director  
Association for Psychological Science

**About the Association for Psychological Science:**

Founded in 1988, the Association for Psychological Science is a nonprofit organization of 33,000 members whose mission is to promote, protect, and advance the interests of scientifically oriented psychology in research, application, teaching, and the improvement of human welfare. APS is an authoritative voice in psychological science, publishing five highly-regarded journals that showcase cutting-edge empirical and theoretical research spanning the entire spectrum of basic and applied areas within the field.