Meeting with Scientific Societies Regarding Basic Research with Human Subjects and NIH Clinical Trials Policies
Wednesday, May 2, 2018

In person:
Paula Skedsvold – Executive Director, Federation of Associations in Behavioral & Brain Sciences (FABBS)
Lisa Nichols – Director, Research & Regulatory Reform, Council of Government Relations
Sarah Brookhart – Executive Director, Association for Psychological Science (APS)
Mike Hall – government relations consultant for APS (Madison Associates, LLC)
James J. Pekar - Kennedy Krieger Institute & Johns Hopkins University
Jennifer Dreyfus – government relations consultant for American Society for Investigative Pathology (Dreyfus Consulting, LLC)

Call in:
Jeremy Wolfe – FABBS / Harvard Medical School
Jennifer Lodge – Washington University in St. Louis
Laura L. Namy - Society for Research in Child Development
Judith Siuciak - American Society for Pharmacology and Experimental Therapeutics
Alyson Lewis -- government relations consultant for APS (Madison Associates)
Howard Kurtzman—American Psychological Association
Patricia Kobor – American Psychological Association

NIH:
Lawrence Tabak – Principal Deputy Director, NIH
Adrienne Hallett – Associate Director for Legislative Policy and Analysis, NIH
Anne Houser – Senior Legislative Analyst, OLPA, OD
Jerry Sheehan – Deputy Director, National Library of Medicine
Nicole Garbarini – Special Assistant to the NIH Principal Deputy Director

The meeting was led by Dr. Lawrence Tabak, Principal Deputy Director for NIH. He began the meeting by noting two principles with which he thought everyone would agree:

- We want to ensure public trust in taxpayer-supported research through transparent and rigorous research practices.
- Participants in NIH-supported studies are valuable contributors to research. We owe them transparency, and we likewise owe them results reported in a timely, accessible manner.

This was agreed upon by the group.

He then articulated three concerns which he believed were the concerns of the group with respect to basic research:

- Concerns about peer review
- Concerns about applying to clinical trial funding opportunity announcements (FOAs)
- Concerns about registration and reporting

Participants indicated that the basic science community has no objection to and voiced support for registration and reporting, but that it needed to be tailored to basic science. Several attendees emphasized that the primary concern is the lumping of basic science with clinical trials results in basic science being subjected to all present and future policies for clinical trials.

The remainder of the meeting discussion revolved around three main themes:

- registration and reporting
- concerns about additional case studies
- the basic scientists represented in the room are disconcerted by their research being newly classified as a clinical trial, and are concerned about added burdens.

Dr. Tabak offered that the Open Science Framework could be an acceptable option for registration and reporting as a portal to ClinicalTrials.gov for some studies. The group expressed a willingness to consider this and other alternatives, though concerns were raised about how burdensome it might be for investigators who conduct multiple small studies to have each of those studies treated as a clinical trial for reporting purposes. The group suggested they would support using something like the Open Science Framework if the details could be worked out. The group felt that if alternative platforms are to be allowed, the nature of the right platform(s) should be discussed with the broader research community. Furthermore, if alternative platforms are to be allowed, what studies to report on which platform should be clear to scientists.

The participants noted that if a fundamental science project is deemed to be a clinical trial, the investigators would be subject to everything a trial investigator would have to do. This would include participation in Good Clinical Practice (GCP). Dr. Tabak noted that this training is freely available and available online, and is a relatively short training (<4 hours) that reinforces good practices for anyone working with human subjects.

The stakeholders represented felt that the revised case studies were expansive interpretations of the words "intervention" and "health outcome" that sweep up much basic research into the category of "clinical trials". The stakeholders explained that NIH's 2017 published "Cases" appear to avoid this historical understanding and instead manifest expansive readings of "intervention" and "health outcomes", in a manner that diverges from NIH's original statement of purpose and previous case studies. It was noted that this inconsistency, and the harm done by the resulting unintended consequences, has caused what feel like concerns regarding trust. Participants noted that they had no issues with the October 2014 clinical trial case studies that corresponded with the revised definition of clinical trials.

The group then moved to discussion of the case studies developed since 2014 and how the case study examples published in 2017 muddied the waters in terms of understanding what then is a clinical trial, and that a clearer framework is needed, rather than differences of opinion being decided by Dr. Lauer. Participants suggested that NIH was effectively broadening the definition of clinical trials through the most recent case studies and noted that the number of studies had more than doubled since those published in October 2014 with the revised definition. Rather than providing clarity, the revised case studies, which are inconsistent with the historical interpretation of clinical trials, have created significant confusion throughout the research community and even within NIH. Dr. Tabak raised the point that many investigators in the basic/behavioral science community already register and report their research on clinicaltrials.gov, to which it was noted this is a tiny fraction of behavioral science.

The group questioned the goal of the moving to the clinical trial FOAs. Dr. Tabak and Adrienne Hallett explained that NIH was required by Congress to be more transparent, and GAO reviews have also made similar recommendations to NIH. They also raised that Congress was specifically asking NIH to report numbers of individuals in all of the studies supported by the NIH, by age (including children), gender, ethnicity, and how it is not possible to provide this information without a reliable data collection framework where these study participants can be counted. Stakeholders suggested that reporting on

participants could happen through a registration and results reporting framework that is tailored to basic science or other mechanisms and that the current approach wouldn't capture the full numbers (i.e., for studies not deemed clinical trials). As well, the Cures Act has not required a redefinition of clinical trials. Ms. Hallett commented that would delay the reporting for 3-5 years. Stakeholders noted that more basic science involving humans would be counted in an Open Science framework, whereas using ClinicalTrials.gov would continue to exclude basic science research that is not defined as a clinical trial.

The group did not support the argument that characterizing their basic research as clinical trials served the goals of transparency, respect, and reporting. They felt that a strong case could be made for the opposite argument, that respecting a distinction between basic research and clinical trials was important for serving the goals of transparency, respect, and reporting.

About this time, the stakeholders raised the topic of the petition sent to NIH in the fall, which was signed by approximately 3,500 individuals. Dr. Tabak raised the context of the broader NIH research community, which includes over 60,000 applicants per year. Even if this group at the May 2 meeting could agree upon something, it does not represent the totality of the stakeholders (a point also mentioned by the invitees at the beginning of the meeting). There was more discussion about what would constitute a consultation with the community, as NIH is also required to do. The group stated that this meeting should not be considered meeting the requirement of community consultation as more input is needed to resolve the issues. The stakeholders recommended an additional RFI and conferences on the topic, or the possibility of asking The National Academies to review the issue and make recommendations. Dr. Tabak countered that a NAS study would be expensive and take a lot of time. Some indicated that they would like to see the Open Science Framework idea move forward in the meantime, but that NIH needs to provide the details/specifics of what registration and reporting under this framework would entail, and that additional input from the basic science community would be needed once the details were available.

One stakeholder asked what NIH was going to do to respond to the congressional report language from the FY2018 Omnibus, that directs NIH to delay for one year "... enforcement of the new policy published in the Federal Register on September 21, 2017 - including NIH' s more expansive interpretation of 'interventions' - in relation to fundamental research projects involving humans," and recommended, for example, sending a letter to extramural staff explaining the policies would not be enforced for basic research studies, in response to this Congressional directive. NIH responded that the policies were not currently being enforced, and the stakeholders asked that that be announced to the scientific community as soon as possible since investigators were working on proposals for the June cycle. Dr. Tabak said that NIH would make an announcement, and that the societies should not do so.

The group understood that NIH needs to be able to identify the broad space of humans participating in NIH-supported research, and this can only occur if investigators are asked to report. The group agreed that human subjects research should be reported. It remains to be determined how fundamental basic human subjects research should fit into this, though a new "front door" to CT.gov such as the Open Science Framework seems to be one possible part of the solution. Also, several paths for reporting the information could be an option. Different types of research (basic behavioral science, neuroimaging, classical clinical trials) could funnel the relevant data into a database like ClinicalTrials.gov through appropriately tailored portals to reduce wasted effort. That issue is still an open question.

The group communicated to NIH that NIH's desire to capture additional human subjects research data should not be addressed by broadening the definition of clinical trials to encompass basic science research that clearly falls outside of a common understanding of the nature of a clinical trial. The group

emphasized that any RFI related to registration and reporting should be separate from the major issue of the overly broad clinical trial definition.

The group communicated to NIH that they favored registering and reporting of *all* NIH-funded research with humans. However, that registration and reporting would need to be appropriate to the type of research. Mandating reporting for human subjects basic science research without expanding the definition of clinical trials, accomplishes both NIH's goal of more comprehensive reporting and the group's goal of avoiding including research that is not testing clinical interventions in the definition of clinical trials. Consequently, they continue to ask that the definition of clinical trials (the clinical trial case studies) be returned to something like its 2014 form and they volunteered to work with NIH to achieve universal reporting of human research.

Dr. Tabak told the group that NIH would:

- Summarize what we heard and share it with the stakeholders.
- Issue a statement on the enforcement of the clinical trial policies (as they relate to basic science only), including, as directed by congressional language, NIH's actions to "delay enforcement of the new policy published in the Federal Register on September 21, 2017 – including NIH's more expansive interpretation of "interventions"-in relation fundamental research projects involving humans."
- Work on what the next steps should be, such as whether there should be another RFI.
- Share the next steps with stakeholders, research institutions, and NIH's internal stakeholders.