Letter to AAHRPP on Inclusive Clinical Trials

Elyse Summers, JD
President and CEO

Stephen Rosenfeld, MD, MBA
Chair, Board of Directors

5335 Wisconsin Ave NW
Suite 510
Washington, D.C. 20015

Dear Ms. Summers and Dr. Rosenfeld,

The undersigned organizations are writing to request that the Association for the Accreditation of Human Research Protection Programs (AAHRPP) consider updating its accreditation guidelines and resources (for Institutional Review Boards (IRBs) seeking accreditation or accreditation renewal) to include information addressing issues of access to, and representation in, clinical trials for all individuals impacted by a specific disease.

As experts in your field, you know that IRBs are guided by three foundational principles as stated in the Belmont Report: a) respect for persons; b) beneficence; and c) justice[1]. According to the US Department of Health and Human Services, IRBs are crucial for "maintaining the public's trust in the research enterprise and allowing science to advance for the common good."[2] While IRBs have historically focused on protecting participants from harm and minimizing risk, the need remains to increase efforts related to the principle of justice, including measures to increase representativeness in the selection of research participants. Consistent with the Declaration of Helsinki (point 13), "Groups that are underrepresented in medical research should be provided appropriate access to participation in research."[3] Inclusion of all demographics impacted by the disease or therapy under investigation, except where scientifically, medically or ethically justified, should be considered an obligate responsibility. As key stakeholders in the clinical trial ecosystem, we believe IRBs should be an important ally in the discussion about access and representation in clinical trials and with their authority, IRBs should hold investigators accountable for the design of trials that thoughtfully reflect patients in the real-world.

As the accrediting body for IRBs, we believe AAHRPP plays a pivotal role in empowering IRBs to implement improved processes in two major areas:

1) **Developing Guidance to Promote the Attainment of Fair and Equitable Selection of Participants**:
   We recommend that AAHRPP create resources on a) how to evaluate and promote, fair and equitable selection of study participants; and (b) additional safeguards that should be included for trials involving vulnerable populations, such as children, prisoners, pregnant women, physically or mentally disabled persons, or economically or educationally disadvantaged persons.

   The AAHRPP IRB evaluation instrument has made some progress in this area. Standard II-3, Element 11.3.C of the AAHRPP standards advises that the "IRB or Ethics Committee has and follows policies and procedures to evaluate the equitable selection of participants," and Standard III-1, Element III.1.E further advises that "[r]esearchers and research staff recruit participants in a fair and equitable manner." The evaluation instrument includes suggestions for requirements, but no guidance on determining when fair and equitable selection has been achieved. The listed elements are expected for all clinical research studies, and do not discriminate equitable from inequitable selection.

This guidance is essential since the US Food and Drug Administration consistently reports low representation of certain demographics in trials for approved therapeutic products, as per the Drug Trials Snapshots Summary Report published from 2020-2024[4] and as such will be of value to IRBs and clinical research investigators.

2) **Providing a Framework to Address Whether and When Payment Constitutes Coercion OR Undue Influence**: We recommend that AAHRPP include as part of its accreditation resources, a practical framework for payments to trial participants that can be used both by IRBs and investigators to combat one of the major barriers to trial participation - the financial burden on participants.

It has been well documented in the literature that the cost of participating in a trial is a key barrier to trial participation.[5,6] Patients participating in clinical trials (especially those from low socioeconomic backgrounds) can experience significant hardships in their trial participation (e.g., lost wages, transportation costs, identifying childcare, etc.). In addition, there are additional hidden or unknown costs of trial participation, such as co-pays for drugs or procedures during the trial. Given these barriers, solutions that promote adequate and appropriate compensation for trial participants are key, and AAHRPP, as an accrediting body, can help IRBs frame that solution for investigators.

The AAHRPP IRB evaluation instrument already has made some progress in this area. Section Standard II-3, Element 11.3.C.1. viii, states that IRBs should have policies and procedures to review proposed participant payments so that they can determine if:

A. The amount of payment and the proposed method and timing of disbursement is neither coercive nor presents undue influence.
B. Credit for payment accrues as the study progresses and not be contingent upon the participant completing the entire study.
C. Any amount paid as a bonus for completion is reasonable and not so large as to unduly induce participants to stay in the study when they would otherwise have withdrawn.
D. All information concerning payment, including the amount and schedule of payments, is set forth in the consent document.

While the above is extremely important and certainly a policy that accredited IRBs do implement, issuing clarity on what payments are considered "coercive or likely to cause undue influence," would be beneficial to provide appropriate guidance to investigators looking to adequately compensate participants in their trials.

To that end, we recommend that AAHRPP include, as part of its accreditation resources, a practical framework for payments to trial participants that can be used both by IRBs and investigators. Resources such as those provided by the Equitable Access to Clinical Trials Project (eACT) or the National Health Council Fair-Market Value (FMV) Calculator tool may be helpful. The framework also should address the need for additional safeguards for vulnerable groups (e.g., children, prisoners, pregnant women, etc.) who are likely to be at further risk of coercion and undue influence (*see*, **21 CFR § 56.111**).[7]

Leveraging insights from published frameworks and the Code of Federal Regulations (*see*, **21 CFR § 56.111**) could be useful in helping AAHRPP develop its own framework and would ultimately help minimize the confusion over the level of compensation that could be considered coercive.

We believe that updating AAHRPP's accreditation guidelines to include the recommendations outlined above will be a critical step in the furtherance of access and representation in clinical trials. Additionally, these updates would help IRBs in their efforts to comply with the current Code of Federal Regulations, would align with both the National Institutes of Health's policies about the inclusion of participants in clinical research, and with the

2024 revisions to the Declaration of Helsinki that cite greater attention to justice and fairness in research, especially as it relates to the inclusion and protection of vulnerable individuals, groups and communities.[8]

Thank you for your consideration of this request. We would welcome the opportunity to partner with you to help make changes in the areas highlighted above.

Sincerely,

American Society of Hematology (ASH
ASH Research Collaborative (ASH RC)
Ain Shams University
Parkinson's Foundation
Agios Pharmaceuticals, Inc
Society for Public Health Education
American Society of Pediatric Hematology/Oncology
Astellas
Versiti
Endocrine Society
Autism Science Foundation
American Society for Pharmacology and Experimental Therapeutics (ASPET)
Sickle Cell 101
American Society of Nephrology
American Society of Human Genetics
Fulcrum Therapeutics
American Medical Association
Association of Pediatric Hematology/Oncology Nurses
National Bleeding Disorders Foundation
WFH
International Association of Sickle Cell Nurses and Professional Associates

References:

1) https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html
2) https://www.hhs.gov/ohrp/education-and-outreach/online-education/human-research-protection-training/lesson-3-what-are-irbs/index.html
3) https://www.wma.net/policies-post/wma-declaration-of-helsinki/
4) https://www.fda.gov/drugs/drug-approvals-and-databases/drug-trials-snapshots
5) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3170068/
6) https://journals.sagepub.com/doi/abs/10.1177/1740774520905596
7) https://www.ecfr.gov/current/title-21/chapter-I/subchapter-A/part-56/subpart-C/section-56.111
8) https://www.cuatrecasas.com/en/global/life-sciences-healthcare/art/the-2024-revision-of-the-declaration-of-helsinki-key-updates-1