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August 6, 2019

Dockets Management Staff
Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Enhancing the Diversity of Clinical Trial Populations-Eligibility Criteria, Enrollment Practices, and Trial Designs; Draft Guidance for Industry; Availability, Docket No. FDA-2019-D-1264

The Association of American Medical Colleges (AAMC) appreciates the opportunity to comment on the FDA's request for comment on the challenges to participation in clinical trials and approaches to enhancing the diversity of clinical trial populations. The AAMC is a not-for-profit association representing all 152 accredited U.S. medical schools, nearly 400 major teaching hospitals and health systems, and more than 80 academic and scientific societies. Through these institutions and organizations, the AAMC represents nearly 173,000 faculty members, 89,000 medical students, 129,000 resident physicians, and more than 60,000 graduate students and postdoctoral researchers in the biomedical sciences.

The AAMC appreciates the FDA's efforts to increase participant diversity in clinical trials and ensure sponsors take meaningful steps to achieve this goal. In furtherance of these efforts, the AAMC offers the following comments and recommendations.

I. Broadening Eligibility Criteria

The AAMC agrees with the FDA that certain populations are "often excluded from clinical trials without strong clinical justification," and broadening eligibility criteria when appropriate and without jeopardizing patient safety, "maximizes the generalizability of trial results and the ability to understand the therapy's benefit-risk profile across the patient population likely to use the drug in clinical practice."

We appreciate the FDA's recommendations on ways to broaden eligibility criteria to ensure certain populations are not unnecessarily excluded from clinical trials and recognize that achieving sufficient diversity requires striking a balance between exclusion and inclusion criteria. It is important for sponsors to recognize that exclusion and inclusion strategies should not be considered as two separate and distinct approaches. Instead, more attention should be given to the scientific and ethical justification for specific exclusion criteria when designing a study and how those decisions may unnecessarily impact and/or limit inclusion practices, including retention and enrollment. **We recommend the FDA work together with sponsors and the patient community to incorporate appropriate ethical and scientific considerations that expand trial participation through broader eligibility criteria.**

The AAMC agrees with the FDA that pregnant women are frequently excluded from clinical trials and sponsors should consider including pharmacokinetic sampling to establish safety risks associated with dosing in women who may become pregnant during a trial and the risks of continued participation. **We encourage the FDA to consider the recommendations contained in the September 2018 report to Congress by the Department of Health and Human Services' Task Force on Research Specific to Pregnant Women and Lactating Women,**¹ discussing the “significant need for training programs that provide instruction in obstetric and lactation pharmacokinetics [...]”²

II. Improving Clinical Trial Enrollment and Retention

Beyond the limitations imposed by narrow eligibility criteria, the FDA acknowledges additional challenges and burdens that may limit participation (e.g., frequent site visits, financial burdens) and proposes several enrichment design strategies to increase diversity and improve enrollment.

While the AAMC supports the strategies proposed in the draft guidance, we recommend that sponsors include in every enrichment strategy, both populations that are underrepresented in research and populations whose communities suffer from health inequities.³ This approach ensures equitable access for populations and subgroups traditionally excluded from clinical trial participation, allowing for a more complete understanding of drug safety and efficacy in a broader population. To achieve this end, it is also important for sponsors to engage a diverse patient pool, including people with lower SES status; lesbian, gay, bisexual and transgender communities; individuals with limited language proficiency; persons with disabilities; and individuals from distinct contextual and geographic communities (e.g., rural populations).

The AAMC also appreciates the FDA's recommendations to make trial participation less burdensome through electronic communication, reimbursement considerations, and opportunities for recruitment at non-clinical sites. However, the suggestions in the draft guidance are limited and should be further developed and expanded with direct input from key stakeholders and patients to better understand the impact of the proposed approaches.

For example, the FDA's recommendation for using electronic communication and social media platforms to reduce the frequency of study visits may in fact “provide investigators with real-time data,” but this recommendation fails to acknowledge that not all populations have access to mobile technology or the financial ability to support the use of such technology for the sole purpose of participating in a study. **As recommended in the draft guidance, if sponsors replace site visits with technology when feasible**

¹ Task Force on Research Specific to Pregnant Women and Lactating Women, *Report to Secretary, Health and Human Services, Congress* (September 2018).

² *Supra* Note 1. “Increasing research expertise in obstetrics and lactation will be essential to power the expansion of scientific knowledge in this area. Due to the limited number of individuals with expertise in obstetric and lactation pharmacology, there is a significant need for training programs that provide instruction in obstetric and lactation pharmacokinetics, pharmacodynamics (PD), pharmacogenomics, and pharmacoepidemiology.” *Id.*

³ See, AAMC Comment Letter, *Evaluating the Reporting of Age, Race, and Ethnicity Data in Medical Device Clinical Studies; Draft Guidance for Industry and Food and Drug Administration Staff* (September 15, 2016). <https://www.aamc.org/download/469650/data/aamclettertoFDA.pdf>

and appropriate, we strongly recommend that the FDA consider that certain populations may not have the technical or financial infrastructure to participate in a trial that replaces those visits with electronic communication or mobile technology. Consistent with the above recommendation, efforts should also account for populations with low literacy or limited English proficiency that may make recruitment, participation, or communication (particularly with electronic platforms) more difficult.

The AAMC in its comments to the FDA on *The Use of Electronic Records and Electronic Signatures in Clinical Investigations*, noted that face-to-face participant / investigator interaction throughout the duration of a clinical trial is equally important as creating opportunities to reduce or replace study visits with technology:

“[e]nsuring opportunities for participant interaction allows for the ongoing exchange of information between the study participant and investigator and creates opportunities for the investigator to answer questions or address concerns that may arise during the course of the clinical investigation.”⁴

III. Community Engagement and FDA’s Efforts to Increase Patient Participation

The AAMC agrees with the FDA that the design of clinical trial protocols and identifying trial recruitment and participation burdens should be done in partnership with patients, patient advocates, caregivers, and other key community stakeholders. This is especially important considering trial design and recruitment challenges may be unique to certain populations, disease groups, and/or clinical trial specific.

We also agree that “community based participatory research promotes the design of clinical research with the assistance of community members and leaders to more effectively meet the needs of potential participants.” **However, it important that community partners are not solely professional advocates selected, trained, or funded, by drug, device and biotechnology companies. Community partnerships should be led by local organizations and leaders who are better positioned to leverage existing positive relationships with minority patient populations, ensuring that recruitment is conducted in a culturally sensitive manner while preserving public trust.** To support these enrollment and recruitment efforts, sponsors must also consider the organizations’ potential need for financial support.

Finally, consistent with the requirements of Section 3002 of the 21st Century Cures Act (Pub L. 114-115), the FDA has taken steps to collect “patient experience data,” and through the Agency’s Patient Focused Drug Development efforts, the Agency has made significant strides toward understanding the integral role

⁴ AAMC Comments: Use of Electronic Records and Electronic Signatures in Clinical Investigations Under 21 CFR Part 11—Questions and Answer; Draft Guidance for Industry; Availability (Docket No. FDA-2017-D-1105), August 21, 2017.

<https://www.staging.aamc.org/download/482250/data/useofelectronicrecordscommentletter.pdf>

patient expertise plays in the regulatory decision-making process.⁵ In the AAMC’s letter to the FDA on *Patient-Focused Drug Development: Collecting Comprehensive Patient Input*, we recommended that “the Office of Patient Affairs [...] play a key role in the internal coordination of the data submitted to the Agency in addition to serving as a central entry point for industry, patients, and other stakeholders.”⁶ **We recommend again here that the FDA use its Office of Patient Affairs to streamline and coordinate its patient engagement efforts so that recommendations such as those proposed in this draft guidance, are not limited to one center (i.e., Center for Biologics and Evaluation and Research) or department within the FDA but have broader application across the Agency.**

The AAMC appreciates the opportunity to comment on this important issue. To the extent the AAMC can help the FDA advance these efforts or provide additional information, please contact me or my colleagues Daria Grayer, JD, MA at (202) 741-5474 dgrayer@aamc.org or Karey Sutton, Ph.D at (202) 828-0601 ksutton@aamc.org.

Sincerely,

A handwritten signature in blue ink, reading "Ross E. McKinney, Jr., MD". The signature is stylized and includes a small circular mark at the end.

Ross E. McKinney, Jr., MD
Chief Scientific Officer

⁵ Patient Focused Drug Development: Collecting Comprehensive and Representative Input; Draft Guidance for Industry (September 2018).

⁶ See, AAMC Comment Letter, Patient Focused Drug Development: *Collecting Comprehensive and Representative Input; Draft Guidance for Industry* (September 11, 2018).

<https://www.aamc.org/download/492188/data/aamccommentletteronpatientfocuseddrugdevelopment.pdf>