ACRO
ASSOCIATION OF CLINICAL RESEARCH ORGANIZATIONS

September 27, 2022

Lauren K. Roth
Associate Commissioner for Policy
Food and Drug Administration, Dockets Management Staff
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: ACRO comment submission on:
Patient-Focused Drug Development: Selecting, Developing, or Modifying Fit-for-Purpose Clinical Outcome Assessments; Draft Guidance for Industry
[Docket No. FDA–2018–N–2455]

Dear Ms. Roth,

The Association of Clinical Research Organizations (ACRO) represents the world's leading clinical research and technology organizations. Our member companies provide a wide range of specialized services across the entire spectrum of development for new drugs, biologics and medical devices, from pre-clinical, proof of concept and first-in-man studies through post-approval and pharmacovigilance research. ACRO member companies manage or otherwise support a majority of all FDA-regulated clinical investigations worldwide. The member companies of ACRO advance clinical outsourcing to improve the quality, efficiency, and safety of biomedical research.

ACRO welcomes this draft guidance document and thanks the FDA for explaining complex concepts in an understandable manner. We are pleased to provide the following comments.

Line 280-283:
The current text in the draft guidance states: *"Fit-for-purpose in the regulatory context means the same thing as valid within modern validity theory, i.e., validity is "the degree to which evidence and theory support the interpretations of test scores for proposed uses of tests" (American Educational Research Association et al. 2014)."*

The current language reflects only one aspect of the term "fit-for-purpose" when used in a regulatory context. FDA's Fit-for-Purpose Initiative provides a pathway for regulatory acceptance of dynamic tools for use in drug development programs and was established in recognition of the evolving nature of these types of drug development tools and the inability to provide formal qualification (i.e., test scores). Additionally, the ICH E6(R3) draft Principles of Good Clinical Practice document (March 2021) states (Principle 7.1) that the *"quality of a clinical trial is considered in this document as fit for purpose. The quality and amount of information generated during a clinical trial should be sufficient to support good decision-making."* This is complemented by Principle 7.2, which states *"Factors critical to the quality of the trial should be identified. These factors are attributes of a trial which are fundamental to the protection of patients, the reliability and interpretability of the trial results, and the decisions made based on these results."* ICH GCP does not, however, require that critical-to-quality factors are validated, but, rather, that they are appropriately monitored and, if necessary, adjusted in a timely manner to ensure maintenance of the quality of the clinical trial. For these reasons, we ask the Agency to consider qualifying the current text as follows:

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> *Fit-for-purpose in the context of this guidance means the same thing as valid within modern validity theory, i.e., validity is "the degree to which evidence and theory support the interpretations of test scores for proposed uses of tests" (American Educational Research Association et al. 2014).*

Line 766-771:
The current draft guidance text states:

> *Similarly, using different collection modes in the same trial (e.g., different modes for different sites) would raise concerns regarding comparability of assessments in the study. In both cases, part of the COA's rationale for using different modes is that whatever measurement error or bias is created by changing mode of assessment will be too small to affect the assessment of the concept of interest. Whether this is reasonable will depend upon the situation and how the adaptation between modes was accomplished.*

FDA has stated that "Ensuring people from diverse backgrounds join clinical trials is key to advancing health equity" (https://www.fda.gov/consumers/minority-health-and-health-equity/clinical-trial-diversity). Unfortunately, there may be a conflict between ensuring that citizens who are not technology-savvy or lack access to necessary IT equipment are not excluded from a clinical trial and ensuring the lack of bias between IT-based and paper-based recording systems for a COA measure. In order to ensure that patient access to clinical trials is not compromised, we recommend an addition to the text to make clear the commitment that technology considerations should not disadvantage potential trial subjects. We recommend the following language for the final guidance:

> *Similarly, using different collection modes in the same trial (e.g., different modes for different patients) would raise concerns regarding comparability of assessments in the study. In both cases, part of the COA's rationale for using different modes is that whatever measurement error or bias is created by changing mode of assessment will be too small to affect the assessment of the concept of interest. Whether this is reasonable will depend upon the situation and how the adaptation between modes was accomplished. However, patients who are unable to use a particular mode of COA assessment should not be excluded from clinical trials and efforts should be made to ensure that error or bias between modes is reduced to a level that has an insignificant effect on the concept of interest.*

ACRO thanks the Agency for the opportunity to provide input on this draft guidance.
Please do not hesitate to contact ACRO (knoonan@acrohealth.org) if we can provide further detail.

Respectfully submitted,

Karen A. Noonan
Senior Vice President, Global Regulatory Policy