ACRO Innovate Advocate Collaborate

December 16, 2024

Heather Stone, Health Science Policy Analyst, CDER
James Myers, Associate Director for Policy, CBER
Food and Drug Administration
10903 New Hampshire Ave., Bldg. 51, Rm. 3348,
Silver Spring, MD 20993–0002

RE: ACRO comment submission: *Integrating RCTs for Drug and Biological Products into Routine Clinical Practice* [FDA-2024-D-2052]

Dear Ms. Stone and Mr. Myers,

The Association of Clinical Research Organizations (ACRO) represents the world's leading clinical research and clinical 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-human studies through post-approval, pharmacovigilance and health data research. ACRO member companies manage or otherwise support a majority of all biopharmaceutical sponsored clinical investigations worldwide and advance clinical outsourcing to improve the quality, efficiency and safety of biomedical research.

General Comments and Recommendations:

ACRO thanks the Agency for releasing the draft guidance on *Integrating Randomized Controlled Trials for Drug and Biological Products into Routine Clinical Practice.* As the Agency notes, these "point of care trials" or "large simple trials" – much like decentralized trials – have the potential to expand participant access to research, as they *"may improve convenience and accessibility for participants and allow for enrollment of more representative populations, resulting in more generalizable trial results. Leveraging established health care institutions and existing clinical expertise in the medical community can reduce startup times and speed up enrollment."*

ACRO welcomes the flexibilities outlined throughout the guidance. First, we are pleased to see that this draft guidance repeats recommendations from the final guidance on *Conducting Clinical Trials with Decentralized Elements* enabling the use of local HCPs to supplement the work of trial staff where it makes sense to do so. The use of local HCPs is appropriate when: (lines 177-178 and 203-208):

- the HCP's tasks do not differ from those that they are qualified to perform in routine clinical practice
- the HCP's tasks require only limited instructions to ensure that they are performed as required
- the HCP's tasks do not:
    - contribute directly and significantly to trial data
    - require trial-specific knowledge
    - require trial-specific training
    - require research expertise
    - require a detailed knowledge of the protocol
    - require a detailed knowledge of the investigational product
    - require a detailed knowledge of the investigator's brochure

Second, we welcome the Agency's flexibility in considering the potential for more streamlined, limited safety data collection in drugs that are already FDA-approved (lines 313-322):

> *Drugs that are already FDA-approved for an intended use have better established safety profiles and are generally more suitable for use in trials integrated into clinical practice than drugs that are unapproved for any use. An approved product's well-characterized safety profile for the approved use may mean that limited collection of safety data for the unapproved use may be appropriate in certain circumstances. For example, when using an FDA-approved drug, it may be appropriate to consider selective collection of safety data, such as serious adverse events, adverse events of special interest, and adverse events that lead to discontinuation of the drug or withdrawal from the trial without the need to collect nonserious adverse events that are already well characterized. Sponsors should consult with the relevant FDA review division to determine whether a selective approach to safety data collection would be appropriate.*

Line-specific comments:

Line 215 and lines 306-309:
ACRO welcomes the support for increased utilization of EHRs in point of care (large simple) trials. This includes clinical data (line 215), consent (line 306), concomitant medications (line 368), lab results (line 414). In particular, ACRO welcomes the potential of using EHRs to support involvement of small community health care facilities that have historically been involved less frequently in FDA-regulated clinical trials (lines 138-141). This could further support clinical trial diversity.

In the discussion of the potential use of EHRs for informed consent, the draft guidance notes scenarios where informed consent could be either within – or outside of – the EHR: *"Informed consent documents for a trial can be embedded in EHRs, akin to how clinical informed consent documents can be embedded in EHRs for patients undergoing surgery or other procedures. Other electronic or paper-based processes for informed consent may also be appropriate* (lines 306-309)*."*

In its discussion of the role of local HCPs in point of care (large simple) trials, the draft guidance notes that an example of a task appropriately delegated to an HCP is *"collecting routine clinical data for the trial (e.g., vital signs) in a template provided in the EHR* (lines 215-216)*."* We ask the Agency to consider refining this to note that, sometimes, an EHR template may reflect data collection requirements for routine care that differ from the data collection requirements for a clinical trial and may exclude pertinent data. ACRO asks the Agency to consider including a statement that – before a point of care (large simple) trial is initiated – the EHR is assessed to identify instances where the relevant data can be collected via the EHR and where additional data collection is needed external to the EHR.

Lines 260-263:
The draft guidance states: *"It may be necessary to supplement data collected from clinical practice with procedures performed by investigators or subinvestigators or other trial personnel when the study procedures cannot be integrated into clinical practice without significant disruption to routine clinical workflows."* While we concur with this recommendation, we ask the Agency to consider refining this recommendation in the final guidance to note that the potential burden to patients should also be taken into account, as this

recommendation may result in the need for patients to grapple with multiple visits at multiple locations. Moreover, this may also risk compliance with the protocol due to the increased complexity of visit schedules. ACRO would therefore recommend the addition of a statement at the end of line 263 such as "To minimize burden for trial participants, study procedures should be integrated into clinical practice where appropriate. Visits to an investigator or sub investigator should be evaluated for feasibility and practicality for participants."

ACRO thanks the Agency for this opportunity to comment on draft guidance on *Integrating Randomized Controlled Trials for Drug and Biological Products into Routine Clinical Practice.*

Please do not hesitate to contact ACRO if we can provide further details or answer any questions (knoonan@acrohealth.org).

Respectfully submitted,

Karen Noonan
Senior Vice President, Global Regulatory Policy