Enhancing Adoption of Innovative Clinical Trial Approaches; Public Workshop; Request for Comments

As part of its mission, the FDA Center for Drug Evaluation and Research (CDER) fosters drug development by providing scientific and regulatory advice and direction. The ecosystem in which CDER fulfills this role is rapidly transforming. Evolving understanding of disease biology and molecular pharmacology, advancements in drug discovery, and growth in novel therapeutic platforms (i.e., beyond small molecule drugs) have the potential to transform the development of promising new therapies for patients with rare and common chronic diseases. These changes in the drug development landscape require novel clinical trial designs and innovative strategies for trial execution, an expanding range of drug development tools, and wider application in regulatory drug development of real-world data sources.

With this changing landscape in mind, CDER has undertaken many efforts to advance innovation in clinical trial design and conduct. From working groups and public workshops, to guidances and trainings, to innovative programs and public-private partnerships – CDER's portfolio of clinical trial innovation activities are wide ranging and span across drug development programs, therapeutic areas, and scientific disciplines. These efforts include (but are not limited to):

- Programs in complex innovative trial designs (CID), model-informed drug development (MIDD), real-world evidence (RWE), rare disease endpoint advancement (RDEA), patient-focused drug development (PFDD), and digital health technologies (DHTs)
- Guidance on implementing decentralized clinical trial (DCT) designs and use of DHTs
- Developing efforts to enhance use of simpler trials that could more easily be integrated into clinical practice (often called "point-of-care trials")
- Artificial intelligence and machine learning in the drug development lifecycle
- Drug Development Tool Qualification Program
- Efforts to improve enrollment of participants from underrepresented populations, including racial and ethnic groups, through innovative clinical trials
- International harmonization efforts related to innovative clinical trial design and conduct
- Public-private partnerships and other external collaborations

These efforts have led to successes in more efficiently designing and conducting clinical trials that demonstrate the value of clinical trial innovations. However, despite the heightened interest and activity, the incorporation of successful or promising innovative clinical trial approaches in drug development programs still appears to be opportunistic and heterogeneous.

CDER is soliciting public comments on the barriers and facilitators to incorporating successful or promising innovative clinical trial approaches in drug development programs. Questions that could be addressed include, but are not limited to, those listed below. It is not necessary to answer all the questions below. Comments submitted to this public docket will inform CDER's future work related to clinical trial innovation and the planning of an upcoming public workshop sponsored by CDER and Duke-Margolis Center for Health Policy on March 19 and 20, 2024. Details about the upcoming workshop titled, *Enhancing Adoption of Innovative Clinical Trial Approaches*, can be found on CDER's meeting webpage and Duke-Margolis' meeting page.

1. What are the key challenges or barriers, perceived or actual, that may hinder the implementation and adoption of innovative approaches in clinical trial design, conduct, and execution? Consider and if applicable, provide specific examples associated with the categories listed below:
    - Regulatory and Compliance Considerations

    - Unknowns regarding the application of new technologies and their successful integration into existing infrastructure or processes Uncertainties regarding the application of FDA regulations and policies to new technologies
    - Adherence to Good Clinical Practices
    - Investigator oversight and responsibilities
    - Data quality
- Patient-Focused Trial Design and Recruitment Innovations
    - Concerns for patient safety
    - Patient recruitment and engagement
    - Informed consent
- Clinical Trial Infrastructure and Organizational Considerations
    - Technical and analytical capabilities (data collection, management, and analysis)
    - Organizational culture in the clinical trial enterprise
    - Insufficient information regarding innovative approaches and how to implement them
    - Capabilities of trial organizations
- Overarching Barriers
    - Collaboration and communication between stakeholders (e.g., sponsors, CROs, sites, networks)
    - Understanding/familiarity with new methodologies and technologies

2. Provide examples of instances where integrating new innovations into existing programs or systems became particularly challenging. Are there specific actions that CDER or others could take to enhance implementation and adoption of innovative approaches in clinical trial design, conduct, and execution?
3. Do certain therapeutic areas or types of trials face unique barriers or challenges to implementing innovative approaches? If yes, please explain.
4. What challenges emerge when trying to apply innovative approaches in new areas (e.g., in a new therapeutic area or different trial types)? What are the considerations that become more important as innovation is scaled and approaches wide-spread implementation? How can stakeholders in the clinical research enterprise address these considerations effectively?
5. What are effective ways to enhance and coordinate communications with CDER (e.g., review divisions, compliance/inspectorate) or across other FDA stakeholders as new clinical trial innovations are implemented? Please describe the specific stakeholders, areas, or aspects that may benefit from enhanced communication or coordination.

The public docket will close on April 19, 2024. Those who wish their comments to be considered in the discussion at the public meeting must submit them by January 19, 2024.