CENTER FOR DRUG EVALUATION AND RESEARCH

Center For Clinical Trial Innovation (C3TI)

Welcome to the second issue of the CDER Center for Clinical Trial Innovation (C3TI) Newsletter, and our first issue of 2025. The start of the calendar year is an opportunity to both reflect and plan for the future, and I am inspired by the significant strides the clinical research community has made in key areas of innovation.

Over the past several years, the agency has issued critical guidances that describe FDA's thinking on clinical trial design elements, which enable greater flexibility and support more diverse and broad-based trials. These include guidances on randomized trials in practice settings, decentralized trials, digital health endpoints, selective safety data collection (based upon an ICH guidance), and a wide range of guidances informing the use of real-world evidence in regulatory decisions.

The guidances have provided an extensive framework allowing for efficiencies and innovative approaches to clinical trial design. The next step is to help drug developers translate these principles and approaches into innovative trials. That is where C3TI comes in — helping drug developers adopt these innovative approaches into trials appropriately and sharing lessons learned from such experiences.

Looking ahead, C3TI will continue to explore the use of pragmatic elements, including real-world data and digital health technologies; advanced statistical methods, such as Bayesian statistics; and artificial intelligence/machine learning in clinical trials. We are interested in further insights into the integration of trials in routine clinical practice, including data capture and electronic health records for safety reporting. In addition, we are looking at inspection processes for innovative trial designs, prioritizing elements that matter most for patient safety and data integrity. Strengthening the feedback loop between sponsors and regulatory authorities, through initiatives like C3TI's Demonstration Program, will help ensure the evolving clinical trial landscape aligns with regulatory expectations and public health needs.

C3TI's goal remains to help the clinical research community stay current with innovations, improve trial efficiency, increase participation from diverse populations in clinical trials, and ultimately accelerate the development of safe and effective treatments.

Wishing you a very happy new year!

Dr. Peter Stein

CDER's Office of New Drugs Director and C3TI Leadership Team Member

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Clinical Trial Innovation News

CDER Establishes New Center for Real-World Evidence Innovation

FDA announced the CDER Center for Real-World Evidence Innovation (CCRI), which aims to coordinate, advance, and promote the use of real-world data and real-world evidence in regulatory decision-making across CDER. CCRI will serve as a collaborative core for innovation and a focal point to ensure CDER promotes consistency and transparency on these topics.

FDA Announces Advancing Real-World Evidence Program Submission Deadline

The deadline for the fifth submission cycle of FDA's Advancing Real-World Evidence (RWE) Program is March 31. For selected product sponsors, the Advancing RWE Program provides the opportunity to meet with FDA staff before protocol development or study initiation to discuss the use of RWE in medical product development.

CDER Podcast Examines Improving Data Quality with Centralized Statistical Monitoring

CDER released a podcast episode focused on improving data quality with centralized statistical monitoring. In this episode, Dr. Paul Schuette and Xiaofeng (Tina) Wang in CDER's Office of Biostatistics discuss their experience with a centralized statistical monitoring tool. Centralized monitoring is a remote evaluation that the sponsor carries out at a location other than the clinical investigation site(s).

FDA Publishes Draft Guidance on the Use of Artificial Intelligence to Support Regulatory Decision-Making

The draft guidance, Considerations for the Use of Artificial Intelligence to Support Regulatory Decision-Making for Drug and Biological Products, provides recommendations on the use of artificial intelligence (AI) to produce information or data intended to support regulatory decision-making regarding drug safety, effectiveness, or quality. This guidance provides a risk-based credibility assessment framework that may be used to establish and evaluate the credibility of an AI model for a particular context of use.

New Draft Guidance Focuses on Sex Differences in Clinical Evaluation of Medical Products

This draft guidance, Study of Sex Differences in the Clinical Evaluation of Medical Products, provides recommendations for increasing enrollment of females in clinical trials, analyzing and interpreting sex-specific data, and including sex-specific information in regulatory submissions of medical products.

FDA Experts Discuss Agency's Role in Revising Declaration of Helsinki, a Set of Ethical Principles for Clinical Research

In an FDA-published interview, FDA Chief Medical Officer Dr. Hilary Marston and Office of Clinical Policy Director Ann Meeker-O'Connell discuss the agency's role in revising the Declaration of Helsinki. The Declaration describes principles that underlie ethical clinical research, such as participant welfare and informed consent. These experts describe how FDA weighed in on important research topics, such as enrollment of vulnerable populations, scientifically sound and rigorous design, and ethical principles during public health emergencies.

CDER and CBER Leaders Discuss the Rare Disease Innovation Hub

CDER Director Dr. Patrizia Cavazzoni and CBER Director Dr. Peter Marks published an FDA Voices piece detailing next steps in establishing a Rare Disease Innovation Hub. The Hub is an FDA cross-center program that will act as the single point of engagement with outside parties and as a forum for CBER and CDER to collaborate on rare disease-related issues. The Hub has also released its Strategic Agenda, which outlines the actions it plans to undertake in its first year.

FDA Hosts Workshop to Discuss Methodological Challenges Related to Patient Experience Data

FDA hosted a virtual public workshop to discuss methodological challenges related to patient experience data, including submitting and evaluating this data in the context of the benefit-risk assessment and product labeling. This workshop explored the different types of patient experience data and how FDA uses such data for regulatory decision-making.

CBER Holds 2nd Meeting about Patient Perspectives on Clinical Trial Enrollment

CBER hosted a second public patient listening meeting and opened a docket to better understand patient and caregiver perspectives on enrollment into gene therapy clinical trials for rare diseases. This meeting aimed to understand what patients in the pre-symptomatic or early disease stages consider when they are deciding to enroll in a clinical trial and potentially receive an investigational gene therapy.

Materials Available from Duke Margolis Meeting on FDA's Real-World Evidence Program

Meeting summary materials are available from the Dec. 12, 2024 Duke Margolis Institute for Health Policy meeting, "Optimizing the Use of Real-World Evidence in Regulatory Decision-Making for Drugs and Biological Products-Looking Forward." This meeting provided an update and solicited input on activities of the FDA's Real-World Evidence program for drug and biologics.

Spotlight: Bayesian Supplemental Analysis (BSA) Demonstration Project

Bayesian statistical approaches can offer different perspectives in assumptions made or addressed for an analysis compared to frequentist approaches. Within the Bayesian Supplemental Analysis (BSA) demonstration project, C3TI will communicate with sponsors on how to use Bayesian methods in supplementary analyses during their trial. This gives CDER and drug developers a chance to learn new methods without impacting review criteria.

The BSA demonstration project is part of C3TI's Demonstration Program, which offers selected sponsors enhanced communication and interaction with CDER staff. This allows sponsors to receive timely and important feedback on the innovation(s) being applied in their clinical trial.

Learn more about the C3TI Demonstration Program.

ICYMI: C3TI on the Road

C3TI staff recently spoke at many in-person and virtual conferences. Interested in requesting a C3TI speaker? Submit a CDER Speaker Request here.

- 11/13/24: International Coalition of Medicines Regulatory Authorities Meeting
- 11/13/24: Decentralized Trials & Research Alliance Annual Meeting
- 11/14/24: Multi-Regional Clinical Trials Center Annual Symposium
- 11/20/24: Pediatric Rheumatology Collaborative Study Group Advisory Council Meeting
- 11/22/24: Reagan-Udall Foundation-FDA Public Webinar

Questions or Comments? Contact C3TI at CDERClinicalTrialInnovation@fda.hhs.gov.
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