CDER Center for Clinical Trial Innovation

U.S. FOOD & DRUG ADMINISTRATION

Center for Drug Evaluation and Research

Bayesian Supplemental Analysis Demonstration Program

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Disclaimer

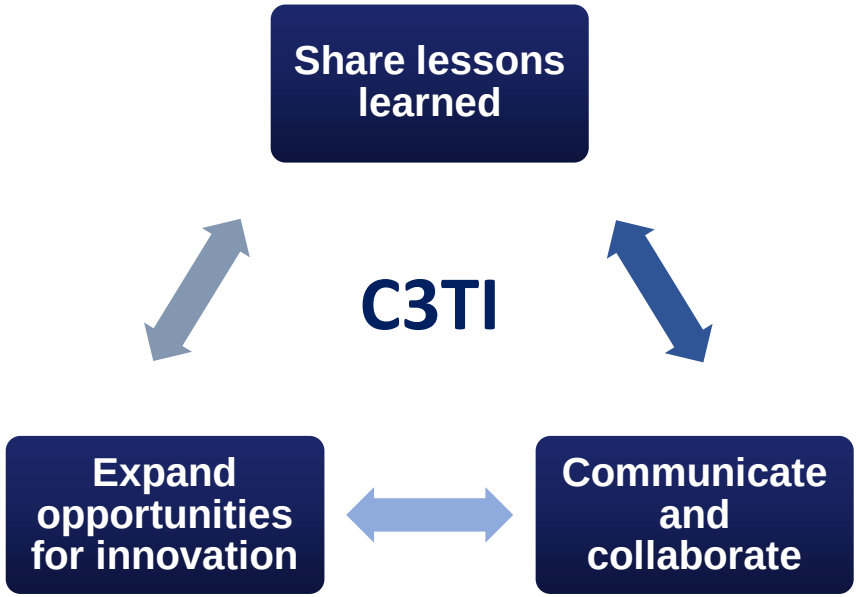
* The views expressed in this talk are those of the speaker and not necessarily those of the FDA

CDER Center for Clinical Trial Innovation (C3TI)

- Central hub supporting innovative approaches to clinical trials that are designed to improve the efficiency of drug development
- Aims to promote existing CDER programs and spur future clinical trial innovation activities through enhanced communication and collaboration
- Enables internal and external parties to access information on clinical trial innovation efforts more easily, engage in collaborations, identify resources that can further support the use of innovative modalities, and identify development programs where a concerted approach to the use of clinical trial innovations would be impactful.

CDER Center for Clinical Trial Innovation (C3TI)

Mission: To promote existing and future CDER clinical trial innovation through enhanced communication and collaboration



Learn more

www.fda.gov/C3TI

CDERclinicaltrialinnovation@fda.hhs.gov

Key Activities:

- Demonstration program to scale adoption of innovation
- Internal and external communication and engagement
- Single point-of-contact for innovation-related questions
- C3TI Compass, a centralized knowledge repository

C3TI Demonstration Program

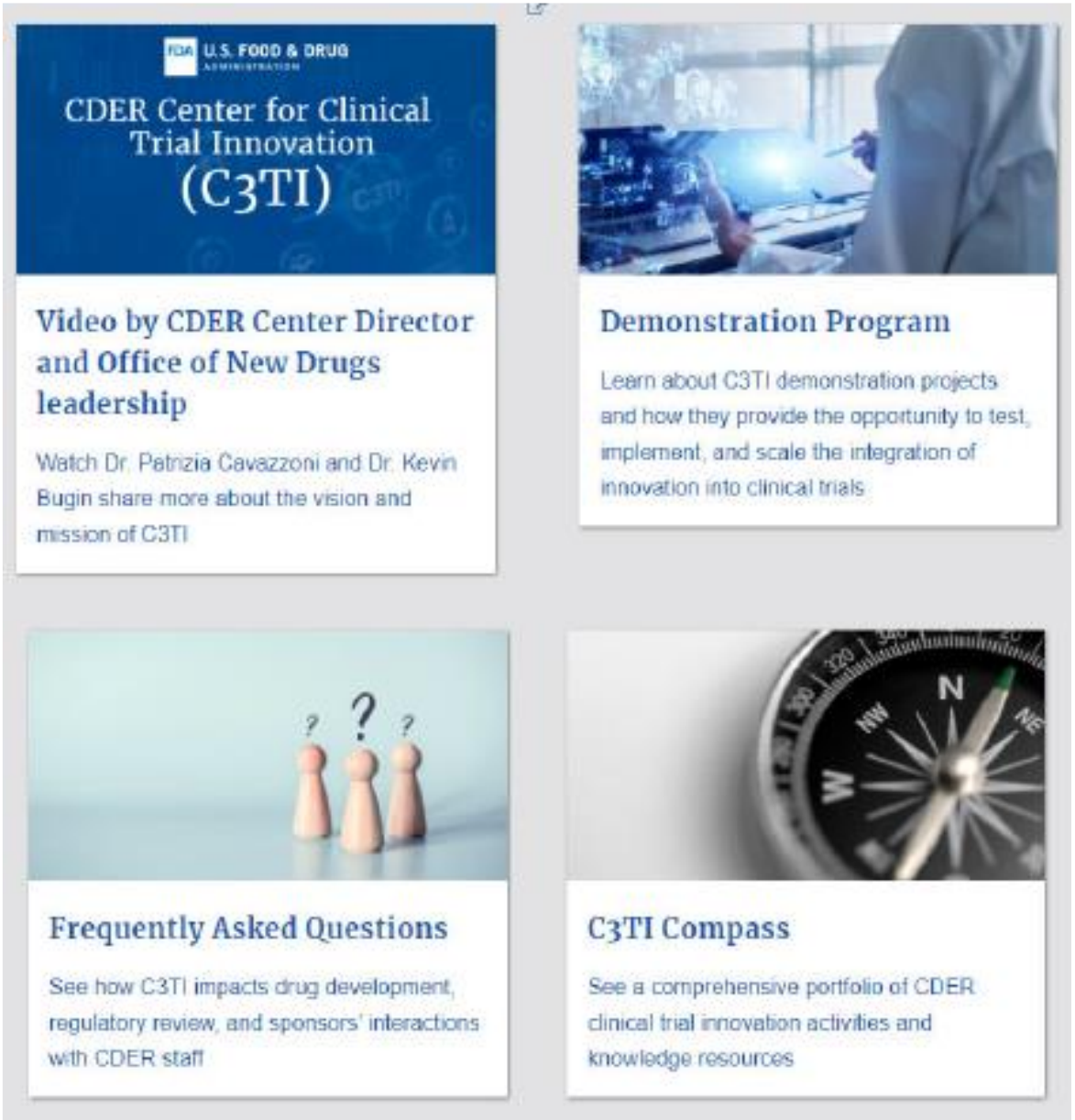
The C3TI Demonstration Program provides the opportunity to **test, implement, and scale select clinical trial innovations.**

- **Increased communication and interaction** among CDER review staff, CDER policy makers, and drug developers.
- **Enables drug developers to explore innovation** in trial design, operational approaches, and data sources while ensuring **FDA's assessment of data quality/reliability focuses on aspects of trial conduct most critical to quality**.
- Supports trials to **serve as case examples** and enhance the body of knowledge.

To learn more about the C3TI Demonstration Program, including proposal eligibility criteria and the submission process, visit www.fda.gov/C3TI.

Goals

- Assist those involved in clinical research in staying current with clinical trial innovations, improve the efficiency and effectiveness of clinical trials, help increase the participation of diverse populations in clinical trials, and, in turn, accelerate the development of safe and effective new drugs.



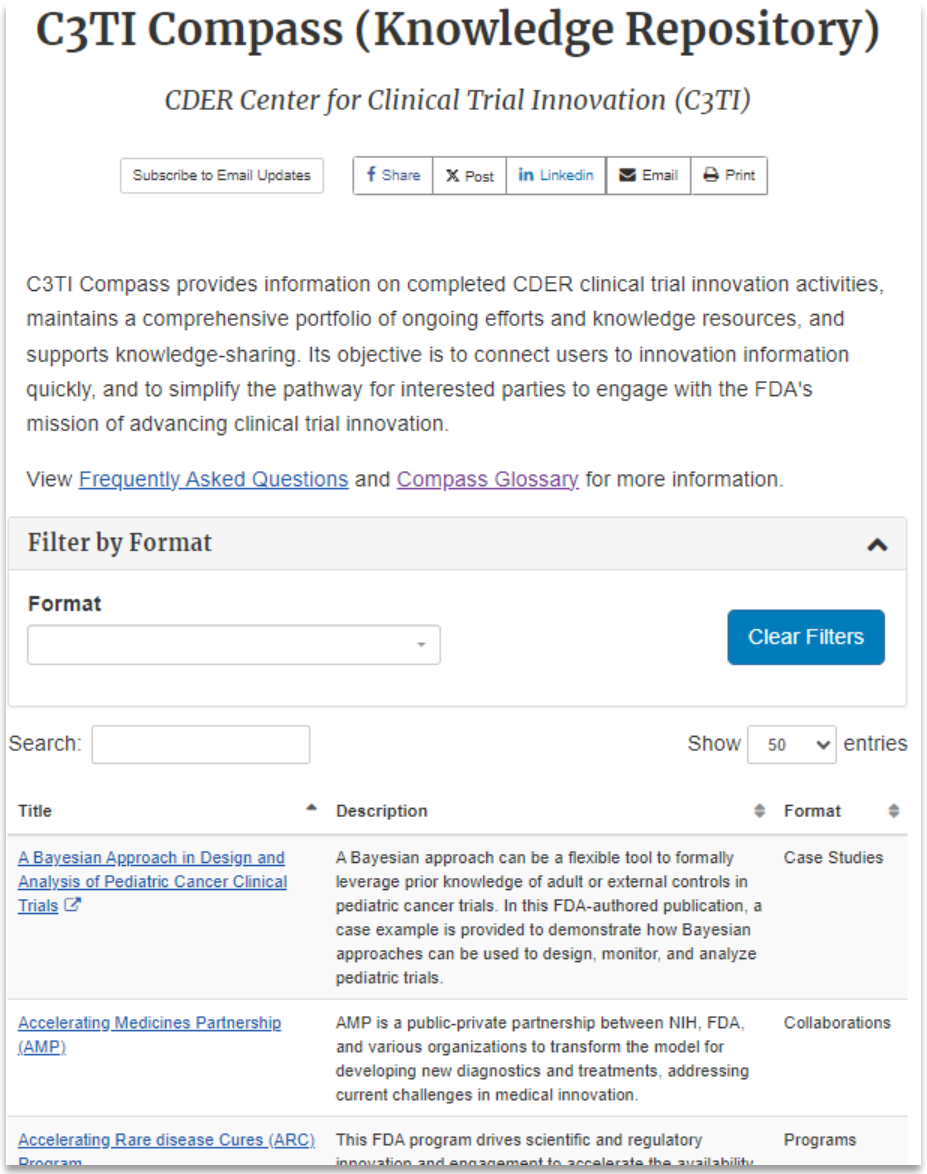
https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/cder-center-clinical-trial-innovation-c3ti

C3TI Compass

A centralized knowledge repository that provides information about clinical trial innovation activities.

- ✓ Searchable platform
- ✓ Curated knowledge, lessons learned, and tools
- ✓ Easily accessible format
- ✓ Regularly updated

Scan QR code or click here to access Compass.



Connect with C3TI!

EMAIL

CDERclinicaltrialinnovation@fda.hhs.gov

WEBSITE

www.fda.gov/C3TI

Coming Soon – C3TI Newsletter!
Sign up today!

Initial Project Areas

Bayesian Supplemental Analysis – Increase CDER staff and drug developers' use of innovative statistical approaches.

Selective Safety Data Collection – Focus on streamlining data collection in clinical trials of drugs with well-known safety profiles to reduce the burden of collecting unnecessary data.

Streamlined Trials Embedded in clinical Practice – Incorporate features such as real-world data collection, decentralized procedures that can be performed in the clinical practice setting, and other innovations to use resources effectively, conduct trials efficiently, and encourage trial recruitment and retention.

BSA Demonstration Project Summary

OBJECTIVES

- Engage 3-5 phase 3 efficacy or safety trials with traditional frequentist designs over the next 3 years
- Educate review teams to understand Bayesian analyses as useful sensitivity/supplemental analyses
- Compare results between Bayesian and frequentist analysis methods, and create reports, including a summary report of all 3-5 trials
- Quantify evidence supporting the demonstration of efficacy, effectiveness, safety, non-inferiority/inferiority, and/or similarity when using Bayesian methods vs. frequentist methods
- *This Demonstration differs from Complex Innovative Designs program in aiming at using Bayesian statistical methods for trials with simple designs.*

GOAL OUTCOMES

- For integrating these approaches into clinical trial design in the future (e.g., processes for pre-aligning on specifications of prior distributions), which would be shared with parties across the drug development landscape to drive appropriate adoption of Bayesian statistical methods
- Improved familiarity with Bayesian methods for sponsors, FDA statisticians, and FDA clinical reviewers.
- Regulatory acceptance of Bayesian methods

C3TI Demonstration Program

Bayesian Supplementary Analysis

- Aims to **increase experience** in Bayesian statistical methods in simple trials settings among sponsors and CDER clinical reviewers and statisticians.
- C3TI will partner with sponsors to use Bayesian methods in supplementary analyses, providing an opportunity for CDER and sponsors to **learn without impacting review** criteria.

Eligibility Criteria

- The sponsor has an active pre-Investigational New Drug (IND) or IND for the product(s) included in the proposal.
- A phase 3 efficacy, safety, or non-inferiority standalone trial (i.e., not incorporating data from previous trials beyond informing the non-inferiority margin) with a simple non-adaptive design.
- The Bayesian analysis should supplement the primary analysis and may be used to evaluate the primary endpoint in the overall study population and/or in relevant subgroups (i.e., for subgroup analysis).

Additional information: Bayesian Supplemental Analysis (BSA) Demonstration Project

BSA Demonstration Project Summary

SPONSOR BENEFITS FOR PARTICIPATING

- Sponsors and other industry parties who are willing to participate in this demonstration project will benefit from demonstrating the value of Bayesian methods in drug development, testing new analytical methods in an experiment-friendly environment without impacting the regulatory decision, and partnering with additional FDA/CDER subject matter experts on Bayesian Statistics.
- Furthermore, by participating, sponsor(s) would receive additional CDER support to reach alignment on the statistical analysis plan for the supplemental Bayesian analysis

Please note that if you know of sponsors who are interested in a trial with a Bayesian primary analysis, please have them email the C3TI Program at **CDERclinicaltrialinnovation@fda.hhs.gov**

Bayesian Supplementary Analysis | Example Statistical Plan

Example Bayesian Statistical Plans Posted to FDA Website

Parallel-Group Trial with a Continuous Outcome	A double-blind trial to assess a drug's effectiveness in lowering acute hypertension in an emergency department setting, utilizing Bayesian analysis to leverage prior medical knowledge and focusing on 2-hour blood pressure reduction.
Supplemental Bayesian Analysis: Unification of Evidence	A double-blind trial with multiple endpoints. A Bayesian approach lets researchers clearly define the specific condition that would change clinical practice and then calculate the likelihood of that condition being met. This condition can be a combination of multiple factors.
Bayesian Subgroup Analysis: Sharing of Information Across Subgroups	This example illustrates how a Bayesian hierarchical model could be used to simultaneously determine estimated treatment effects (via hazard ratios) across four regions for a time-to-event endpoint. Data from all four regions are used in estimating each region-specific hazard ratio.

Program mailbox

- Please note that sponsors who are interested in a trial with a Bayesian supplemental analysis may reach out to C3TI through the program mailbox to be directed to the proper subject matter experts for support.

BSA Demonstration Project Summary

VALUE PROPOSITION

Sponsors

Risk-Free Experimentation: Safe environment to test and demonstrate the value of Bayesian methods alongside frequentist approaches.

Enhanced Data Interpretation: Utilize Bayesian methods to gain a more comprehensive understanding of trial data.

CDER

Enhanced Analytical Capability: Gain a deeper understanding of Bayesian methods, including their application, benefits, and limitations**.**

Regulatory Innovation: Stay at the forefront of statistical innovation by incorporating cutting-edge methodologies.

Improved Collaboration: Align more effectively with sponsors on trial design and analysis, especially in specifying prior distributions.

Thank you!