Innovation in Clinical Trials: What has been achieved with CCTs and key challenges that need addressing

Christine Fletcher
VP Biostatistics, GSK

Disclaimer

The views expressed herein represent those of the presenter and do not necessarily represent the views or practices of GSK.

Agenda

- Innovation in clinical trials
- Key highlights from Complex Clinical Trials (CCT) workshop
- Accelerating Clinical Trials in Europe (ACT EU)
- Linking CCT workshop findings with ACT EU and key challenges to address
- Conclusions

Innovation in Clinical Trials

Innovation in clinical trials

Increase collaboration, flexibility, mutual recognition and reliance among regulators and other stakeholders

Equity in access and awareness
- Improve access and build trust
- Improve awareness of CTs
- Improve acceptance

Innovation, efficiency and speed
- Parallel processing at risk
- Sponsor's knowledge sharing
- Collaboration amongst sponsors

adaptive designs and master protocols

Adaptive and flexible approach
- Using RWE/RWD
- Large pragmatic trials

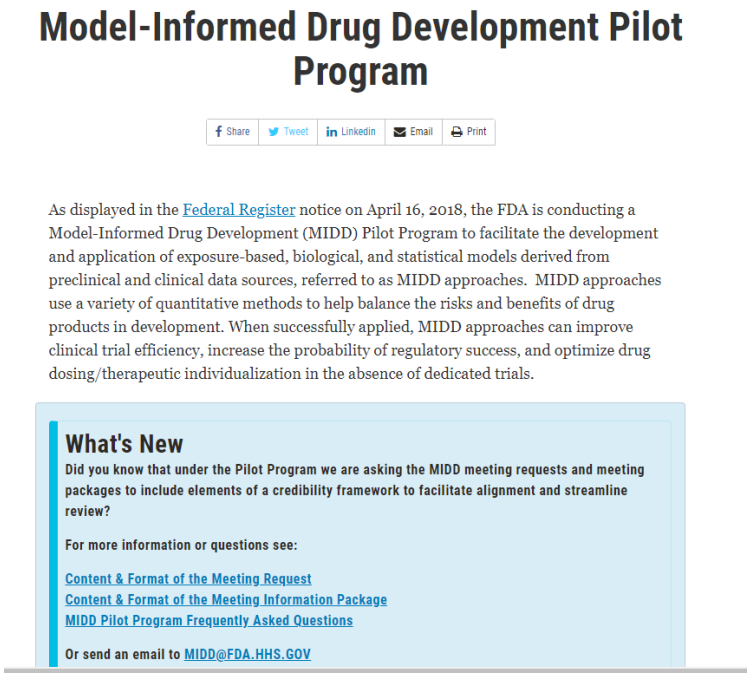
Efficiency and convenience
- Improved clinical operations
- Decentralised clinical trials
- Embrace digital tools

Harmonisation in requirements for innovation in clinical trials

- **Adaptive Clinical Trials – ICH E20** – principles for the regulatory review of these studies in a global drug development program, i.e. design, conduct, analysis, and interpretation (expected 2023)
- **Good Clinical Practice Renovation - ICH E6(R3)** – increasing diversity of clinical trial designs and data sources (adopted by ICH April 2021)
- **Paediatric Extrapolation – ICH E11A** – study designs and statistical analysis methods used when incorporating paediatric extrapolation into a paediatric drug development plan (expected 2022)
- **MIDD – Model Informed Drug Development / Modelling & Simulation (M&S):** ICH MIDD Discussion Group recently established to develop an ICH MIDD guideline.

FDA MIDD and CID pilots

Opportunities to innovate and accelerate clinical development



Model-Informed Drug Development Pilot Program

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As displayed in the Federal Register notice on April 16, 2018, the FDA is conducting a Model-Informed Drug Development (MIDD) Pilot Program to facilitate the development and application of exposure-based, biological, and statistical models derived from preclinical and clinical data sources, referred to as MIDD approaches. MIDD approaches use a variety of quantitative methods to help balance the risks and benefits of drug products in development. When successfully applied, MIDD approaches can improve clinical trial efficiency, increase the probability of regulatory success, and optimize drug dosing/therapeutic individualization in the absence of dedicated trials.

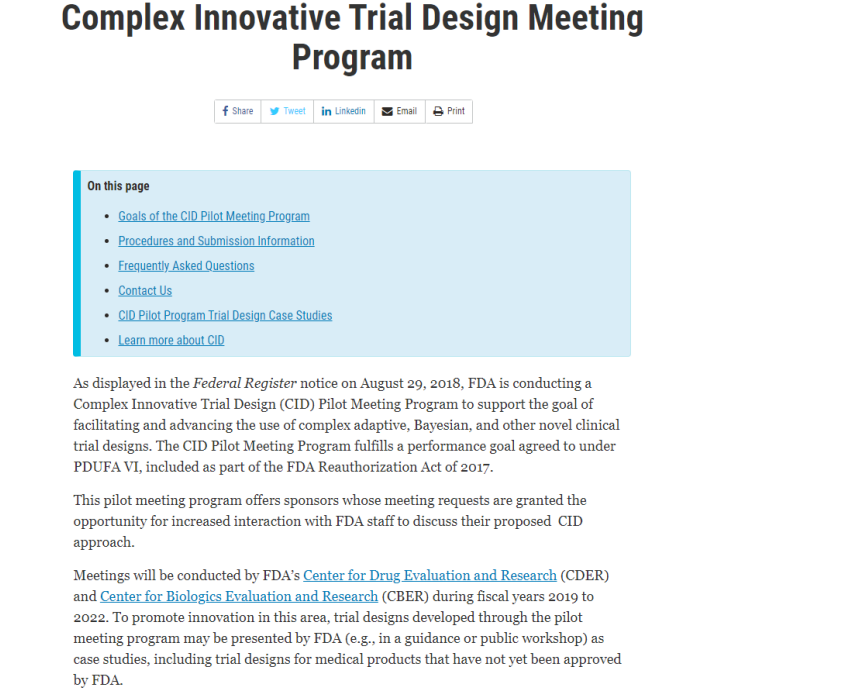
What's New

Did you know that under the Pilot Program we are asking the MIDD meeting requests and meeting packages to include elements of a credibility framework to facilitate alignment and streamline review?

For more information or questions see:

Content & Format of the Meeting Request
Content & Format of the Meeting Information Package
MIDD Pilot Program Frequently Asked Questions

Or send an email to MIDD@FDA.HHS.GOV



Complex Innovative Trial Design Meeting Program

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On this page

- Goals of the CID Pilot Meeting Program
- Procedures and Submission Information
- Frequently Asked Questions
- Contact Us
- CID Pilot Program Trial Design Case Studies
- Learn more about CID

As displayed in the *Federal Register* notice on August 29, 2018, FDA is conducting a Complex Innovative Trial Design (CID) Pilot Meeting Program to support the goal of facilitating and advancing the use of complex adaptive, Bayesian, and other novel clinical trial designs. The CID Pilot Meeting Program fulfills a performance goal agreed to under PDUFA VI, included as part of the FDA Reauthorization Act of 2017.

This pilot meeting program offers sponsors whose meeting requests are granted the opportunity for increased interaction with FDA staff to discuss their proposed CID approach.

Meetings will be conducted by FDA's Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER) during fiscal years 2019 to 2022. To promote innovation in this area, trial designs developed through the pilot meeting program may be presented by FDA (e.g., in a guidance or public workshop) as case studies, including trial designs for medical products that have not yet been approved by FDA.

Key highlights from Complex Clinical Trials (CCT) workshop

Increased alignment on trial design needed between regulatory and HTA agencies

Accelerating Adoption of Complex Clinical Trials in Europe and beyond (efpia.eu)

NF Patients United | efpia European Federation of Pharmaceutical Industries and Associations | BRC | PPD | Norwegian Medicines Agency

CCT Workshop Summary

1. Ensure patients are part of the whole process and are involved early
2. Separate general clinical trial challenges from the challenges specific to master protocols to advance the field
3. Explore the use of master protocols in confirmatory settings as multi-sponsored studies
4. Increase alignment on trial design across regulatory agencies and HTA agencies
5. Develop efficient knowledge sharing platforms between all the key players (academics, sponsors, regulators, HTAs) to share the learnings and discuss how to advance the field
6. Manage clear accountability by careful agreement upfront

Accelerating Clinical Trials in Europe (ACT EU)

Accelerating Clinical Trials in the EU (ACT EU)

ACT EU is an initiative to **transform the EU clinical research environment** in support of medical innovation and better patient outcomes.

- **Builds on the momentum** of the Clinical Trials Regulation and CTIS
- **Driven by** the Network Strategy to 2025 and the EU Pharmaceutical Strategy
- Launched 13 January 2022
- Read the press release and paper

ACT EU Priority actions and domains 2022-2023

Governance & Integration

1. Develop a **governance rationalisation strategy** (aligning different expert groups and working parties)

7. Reinforce the **coordination** between **scientific advice on CT approval and CT design** and link to the methodologies working party domain.

9. Successfully establish **CT safety monitoring** and bridge to the EU4Health Joint Action and start its integration into a pre- and post-marketing safety monitoring framework.

Engagement

3. Establish a **multi-stakeholder platform**, including patients, after stakeholder analysis.

6. Plan and launch a targeted **communication campaign** to engage all enablers.

10. Deliver a clinical trials **training curriculum** on drug development and regulatory science with links to SMEs & academia.

Methods & Practice

4. Implementing the **GCP modernisation** informed by the development of guidance at ICH.

8. Develop and publish key **methodologies guidance** e.g. on AI/ML impacted CTs, complex trials, decentralised CTs and IVDR/CTR interface (to strengthen links between innovation and scientific advice fora).

Impact

2. The successful and timely **implementation of the CTR** and its implementing acts.

- **KPIs** to track performance of the European CT environment.
- **Promote larger, multinational trials** specifically in academia

5. **Analyse data about clinical trials** leveraging academic, non-profit, European, and international initiatives, improving the impact of policymaking and funding to support evidence-based decision making.

Linking CCT workshop findings with ACT EU and key challenges to address

Feedback and challenges identified during the CCT workshop link very well with ACT-EU priorities

CCT Workshop

- change from a drug-centric to a systematic patient-centric approach to trial design
- seek wide consensus on definitions and terminology to facilitate wider understanding
- ensure early formulation of the trial objective, endpoints and key design aspects, identify what data will be needed, and explain the process clearly
- explore CCT opportunities in rare disease and paediatric trials
- explore CCT opportunities in confirmatory settings in multi-sponsor studies
- ensure early agreement on clear accountability, governance, liability and IP protection in multi-sponsor studies

ACT-EU priorities

- 8. Develop and publish key methodologies guidance e.g. on AI/ML impacted CTs, complex trials, decentralised CTs and IVDR/CTR interface (to strengthen links between innovation and scientific advice fora).

Feedback and challenges identified during the CCT workshop link very well with ACT-EU priorities (cont.)

CCT Workshop	ACT-EU priorities
– Training – encourage training and alignment on trial-design principles across regulatory agencies, HTA agencies, and other stakeholders – maximise learning among all stakeholders, with experience-based common templates	– 10. Deliver a clinical trials training curriculum including modules on drug development and regulatory science with links to universities and SMEs (serving as an educational 'ecosystem').
– Collaboration – ensure early engagement with patients, regulators and HTA in trial design, and consistently throughout trial execution	– 3. Establish a multi-stakeholder platform, including patients, after stakeholder analysis.
– Need to have HTAs informed and involved – Dialogue – establish agile and comprehensive collaboration and neutral platforms for knowledge-sharing and pilots, including at global level	– 6. Plan and launch a targeted communication campaign to engage all enablers (including data protection experts, academia, SMEs, funders, HTA bodies, healthcare professionals).
– clearly distinguish advice, collaborative discussion, and approval activities in regulatory discussion	– 7. Reinforce the coordination between scientific advice on CT approval and CT design and link to the methodologies working party domain

Conclusions

All stakeholders need to align on innovation in clinical trials

1. Innovation in clinical trials, such as complex clinical trials, is key for accelerating drug development
2. CCT workshop enabled range of stakeholders to share CCT experiences and align on key areas of focus
3. Many of the workshop learnings are included in the '*Accelerating Clinical* Trials in Europe' initiative
4. The clinical trial landscape continues to evolve and advance at pace
5. Continuous multi-stakeholder interaction and harmonisation will be key to advance this field