U.S. FOOD & DRUG ADMINISTRATION

Public Stakeholder Meeting on Prescription Drug User Fee Act (PDUFA) Reauthorization

October 30, 2020

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Outline for this meeting

- Welcome and Roll Call
- Presentation Topics:
  - Patient Focused Drug Development
  - Model-Informed Drug Development
  - Complex Innovative Designs for Clinical Trials
  - Other Areas of Regulatory Science: Advancing Translational Models & Tools
- Topics for upcoming meetings

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Complex Innovative Designs (CID) for clinical trials

October 30, 2020

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Food and Drug Administration

Complex Innovative Designs (CID) : Background

- Complex Innovative Designs (CID) refers to complex adaptive, Bayesian and other novel clinical trial designs
- CID has the potential to increase trial efficiencies:
  - Decrease number of patients, Accelerate product development, Optimize product development
- Prior to PDUFA VI, limited use of CID intended to provide substantial evidence of effectiveness
  - Lack of uniformity of acceptance and guidance
  - Lack of experience and understanding across industry and FDA
  - Computational complexity
  - Inability to publicly discuss any CID proposals under INDs

CID: PDUFA VI Reauthorization Performance Goals

- Develop staff capacity to enable processes to facilitate appropriate use of CID
- Conduct a pilot program for highly innovative trial designs for which analytically derived properties may not be feasible, and simulations are necessary to determine trial operating characteristics.
  - Pilot includes a pair of meetings, 120 days apart
  - FDA selects up to 2 proposals quarterly each year
  - **To promote innovation, trial designs may be presented by FDA as case studies, including while the drug studied in the trial has not yet been approved by FDA**
- Convene a public workshop
- Publish draft guidance on complex adaptive designs

CID : Progress-to-Date

- Developed staff capacity
  - Launched internal training series
- Launched CID Pilot Meeting Program
  - Published FRN outlining eligibility criteria, content of meeting packages, and disclosure categories – (*August 2018)*
  - Developed a CID website
  - Shared learning through staff participation at over 10 conferences/workshops

CID: Progress-to-Date Pilot Meeting Program

- Accepted 5 of 12 submissions
- Submissions spanned several therapeutic areas
  - Neurology
  - Analgesia
  - Rheumatology
  - Oncology
- Designs Featured
  - Use of Bayesian methodology
  - Formulation of a master protocol
  - Incorporation of external data
- Reasons for denials
  - Lack of therapeutic-area consensus on endpoint
  - Additional interactions would add little value to extensive advice already received
  - Low level of innovation

CID: Progress-to-Date

- Conducted CID Public Workshops
  - Promoting the Use of Complex Innovative Designs in Clinical Trials – (*March 2018)*
  - Advancing Complex Innovative Clinical Trial Designs to Efficiently Deliver Medicines to Patients (*March 2020, in collaboration with DIA*)
- Published guidance documents
  - Adaptive Designs for Clinical Trials – (*finalized November 2019*)
  - Interacting with the FDA on Complex Innovative Trial Designs – (*draft September 2019*)

CID: Summary

- Goal of CID is to bring safe and effective products to patients
- CID has the potential to increase trial efficiencies:
  - Decrease number of patients
  - Accelerate product development
  - Optimize product development
- CID has broad utility but may be particular useful in challenging therapeutic areas
- CID efforts aimed at advancing innovation through collaboration, education, and clarity