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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Model Informed Drug Development (MIDD)

October 30, 2020

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Food and Drug Administration

Advancing Model-Informed Drug Development (MIDD)

Background:

- Development and application of exposure-based, biological, and statistical models derived from preclinical and clinical data sources to address drug development or regulatory issues

- MIDD can improve efficiency in drug development and address residual regulatory uncertainty

- Prior to PDUFA VI, application of MIDD principles were not routinely integrated into drug development
  - Lack of consistent application and uniformity of acceptance
  - Absences of best practices and contemporary guidance to make FDA expectations transparent
  - Unknown resource needs for FDA

MIDD - What was committed to in PDUFA VI?

- FDA will develop its regulatory science and review expertise and capacity in MIDD approaches
- FDA will convene a series of workshops to identify best practices for MIDD. Topics include physiologically-based pharmacokinetic modeling, design analysis and inferences from dose-exposure-response , disease progression model development, immunogenicity
- FDA will conduct a pilot program for MIDD approaches. For sponsors participating in the pilot program, FDA will grant a pair of meetings specifically designed for this pilot program. FDA will select 1-2 proposal per Center per quarter
- FDA will publish draft guidance, or revise relevant existing guidance, on model-informed drug development
- FDA will develop or revise, as appropriate, relevant MAPPs or SOPPs, and/or review templates and training, to incorporate guidelines for the evaluation of MIDD approaches

https://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM511438.pdf

MIDD – PDUFA VI Experience

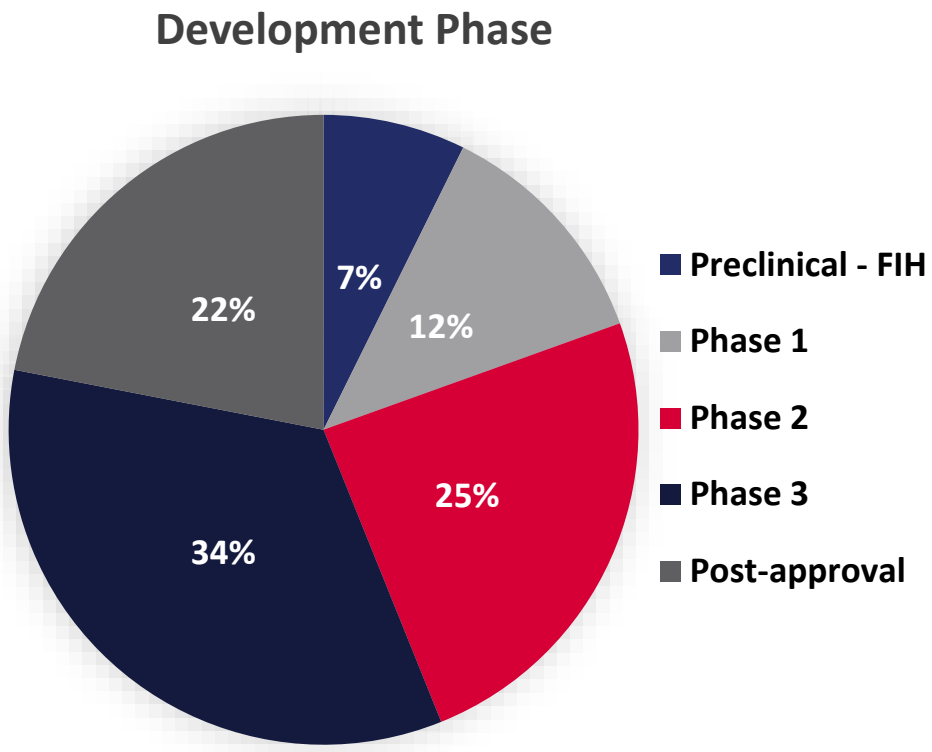
- **Conducted two MIDD Public workshops**
  - Design Analysis and Inferences from Dose-Exposure-Response (2018) ✓
  - Physiologically Based Pharmacokinetic Modeling (2019) ✓
  - Disease Progression Model Development – Planned for 2021
  - Immunogenicity – Planned for 2021
- **Published two MIDD Guidance Documents**
  - Physiologically Based Pharmacokinetic Analysis – Format and Content (*De novo*; Final – 2018) ✓
  - Population Pharmacokinetics (Revised 1999 guidance; Draft – 2019) ✓
  - SOP for Population Pharmacokinetic Analysis (On track to be established in 2020-21)
- **Launched MIDD Paired Meeting Pilot Program**
  - Published FRN outlining the eligibility criteria and procedures for submission (2018) ✓
  - Established a cross-center MIDD Selection Committee to review meeting requests (2018) ✓
  - Operationalized the MIDD Paired Meeting Pilot Program (2018) ✓

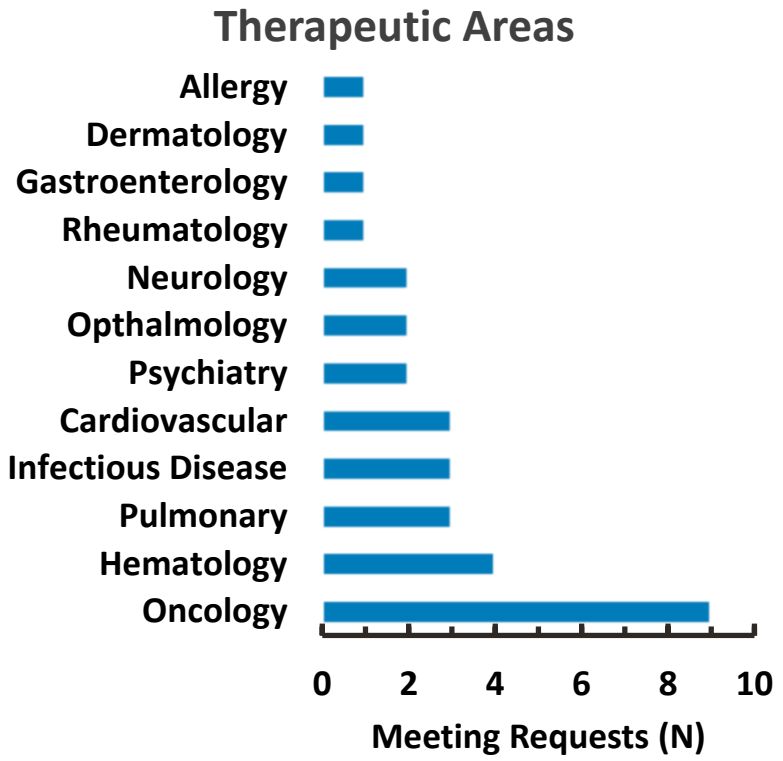
MIDD Website - https://www.fda.gov/drugs/development-resources/model-informed-drug-development-pilot-program

MIDD – PDUFA VI Experience

MIDD Paired Meeting Pilot Program experience

- Received 32 meeting requests (19 different sponsors) over 9 quarters
- Granted 28 meeting requests (~3/quarter)
- Facilitated 2 regulatory submissions





Advancing Model-Informed Drug Development

- Creating an environment that increases stakeholder acceptance of MIDD approaches
- Developing standards and best practices that lead to consistent application and evaluation
- Increasing capacity and expertise to address growing demands and innovation