Model-Integrated Evidence (MIE) Industry Meeting Pilot Program for Generic Drugs: First-Year Review

Advancing Generic Drug Development 2024: Translating Science to Approval

Day 2, Session 6: Ensuring Efficient and Consistent High Quality Generic Drug Development

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Disclaimer

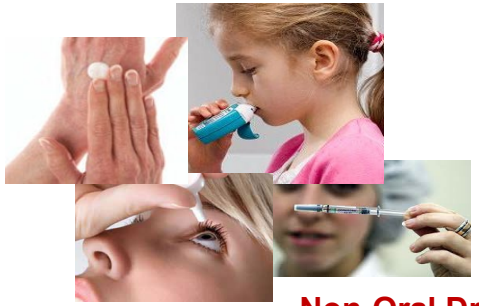
This presentation reflects the views of the author and should not be construed to represent FDA's views or policies.

Learning Objectives

- Provide an overview of model-integrated evidence (MIE) industry meeting pilot program
- Share what FDA has learned through the first year of MIE meeting pilot program
- Recognize potential topics for discussion through the MIE meeting pilot program
- Learn how to prepare an effective MIE meeting request package

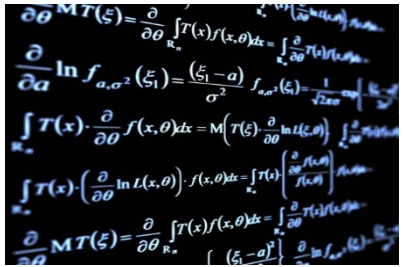
Quantitative Methods and Modeling in Office of Generic Drugs

PK – pharmacokinetics
PD – pharmacodynamics
PBPK – physiologically based PK
CFD – computational fluid dynamics
QCP – quantitative clinical pharmacology

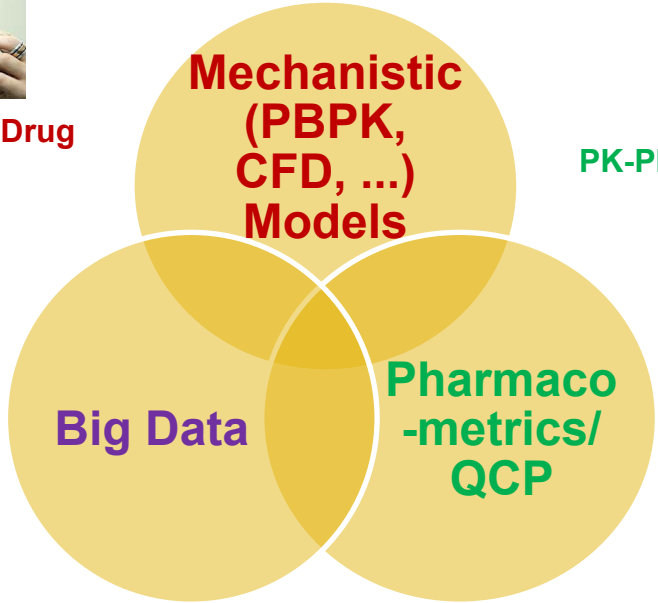


Non-Oral Drug

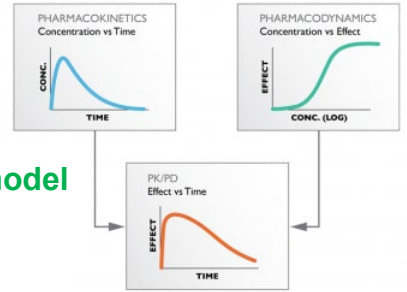
Oral Drug

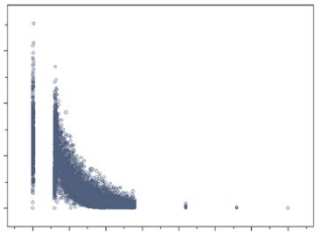


Machine learning toolsets
Analytics for complex mixtures
Systems pharmacology
Risk-based models
Business process models



PK-PD model





Population based model

Slide adapted from SBIA Presentation by Liang Zhao, Ph.D., MIE Industry Meeting Pilot Program for Generic Drugs: Introduction. 1/18/2024

MIE Pilot Program

Launched on October 1st, 2023

The pilot program allows enhanced scientific communications on a broad range of quantitative methods and modeling techniques to address generic drug development issues or questions that are either out of the scope of or cannot be sufficiently addressed by the existing pre-ANDA and ANDA scientific meetings. E.g.,

- Common modeling issues across multiple products
- Complex modeling approaches for non-complex products

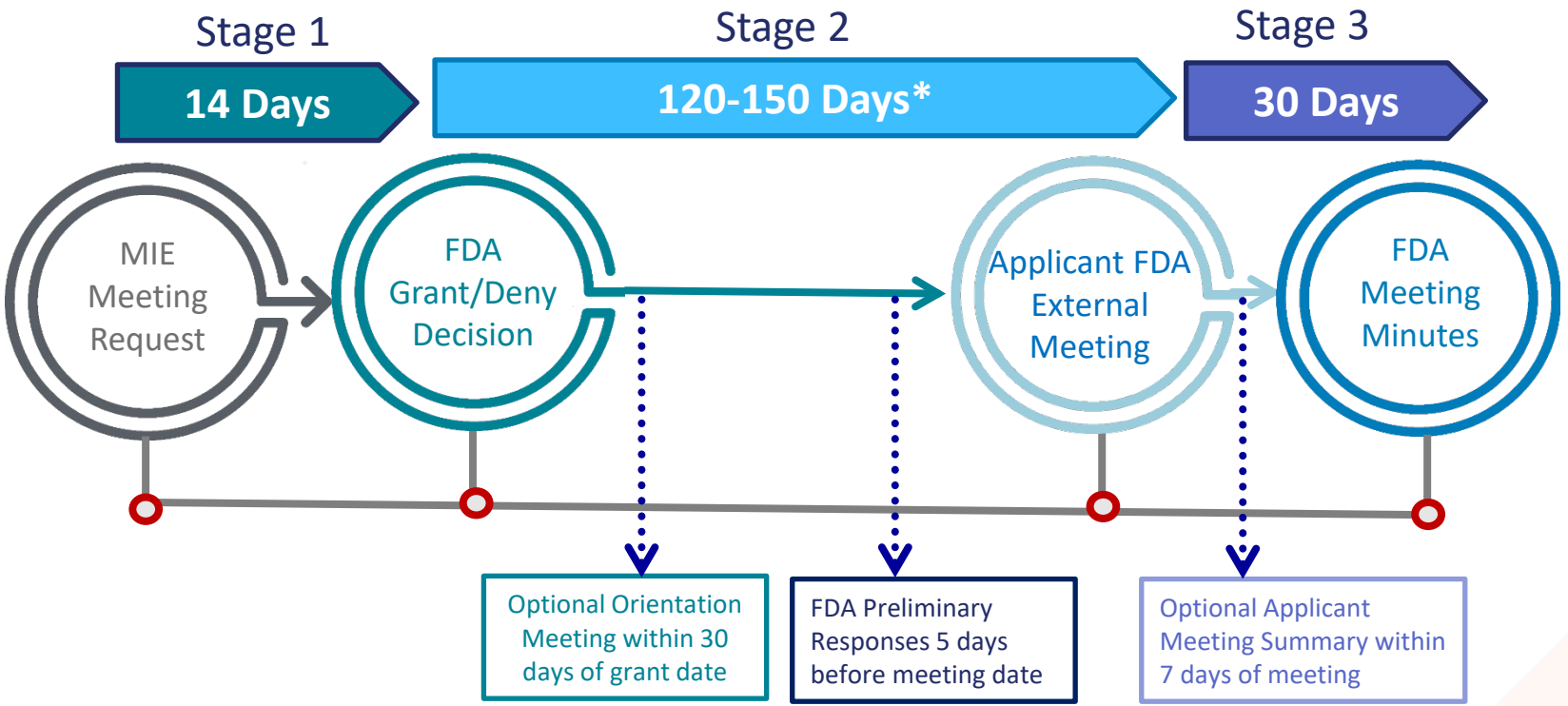
A dedicated regulatory platform for interactions on MIE

- To foster early and focused interactions between industry and FDA on MIE approaches for establishing bioequivalence (BE) in generic drug development

Situations that A Meeting May Be Granted

- Innovative MIE-focused approaches for BE establishment that cannot be effectively addressed under the existing GDUFA scientific meetings
- Non-complex products with complex modeling approaches
- Novel data analytics tools and approaches (e.g., machine learning and artificial intelligence) for BE establishment and assessment

MIE Pilot Program Timeline



*Dependent on optional orientation videoconference

First Year Program Experience - Case 1

- This meeting discussed a complex regulatory issue where modeling and simulation were used to characterize PK differences between available and discontinued products, providing a scientific bridge for BE demonstration under the circumstance where neither the RLD nor the RS is accessible.
  - E.g., Model-based bridging between two oral dosage forms
- The MIE meeting provided in-depth technical discussion regarding data source, bridging strategy, and modeling techniques. A feasible model-based scientific bridging approach was established via this MIE pilot meeting.
- The MIE meeting program allowed to discuss modeling approaches for non-complex product

RLD – reference listed drug; RS – reference standard

First Year Program Experience - Case 2

- This meeting discussed an alternative MIE-focused approach for BE establishment for a long-acting injectable
  - Mechanistic PBPK modeling informed by in vitro characterization data and a small-scale in vivo validation study
  - To reduce the recruiting burden for patients
- Example topics discussed in the meetings
  - Detailed technical discussion regarding modeling method and model validation strategy
  - In vitro experimental methodologies for PBPK model development and validation purposes
  - Approach for virtual BE analysis (e.g., selection of subjects, power of study, variability) and risk assessment (e.g., type I and II error analysis)

What We Learned

- Since launch, two meetings were granted and completed the MIE process.
- MIE pilot meeting provided a unique forum for FDA and industry scientists to gain a shared understanding on model development, model performance, and the use of modeling to address a specific issue in generic drug development.
- FDA participation in the MIE Pilot Program were multidisciplinary.
  - Inputs from OGD/ORS/DQMM-led multidisciplinary review team
  - Alignment in MIE strategy across the FDA review team and with the applicant at early stage
- An orientation meeting was helpful to understand the proposal at early stages and enhance mutual understanding. The video meeting format was especially beneficial as it allows direct communication with the applicant for efficient communication on the complex modeling questions.

Examples of Good Candidates for MIE Meetings

- Innovative MIE-focused approaches for BE establishment to address complex issues for a single product or multiple products
  - E.g., Common strategies for validating a CFD model/platform towards predicting regional deposition for orally inhaled drug products (OIDPs); Alternative study designs for long-acting injectables supported by MIE
- Non-complex products with complex modeling approaches
  - E.g., Modeling for Biopharmaceutics Classification System (BCS)-based biowaivers and/or other study waivers; Model-based bridging to alternative product when RLD/RS is discontinued
- Novel data analytics tools
  - E.g., Equivalence analysis of complex particle size distribution (PSD); New quantitative approaches for sameness assessment; Application of machine learning and artificial intelligence for BE establishment

See details in SBIA Presentation by Andrew Babiskin, Ph.D., Potential Topics for Discussion Through the MIE Industry Meeting Pilot Program, 1/18/2024

Prepare An Effective MIE Meeting Request Package

- Sufficiently developed scientific proposal
  - Meeting questions are relevant, critical, and clearly stated
- Adequate documentation of the modeling approach
  - Purpose of the MIE approaches and how it will be used to address the question of interest and inform regulatory decision-making
  - Sufficient details for underlying assumptions and model building process
  - Clear model verification and validation strategies including current and future data support
  - Risk analysis/assessment
  - Model files and supporting datasets

See details in SBIA Presentation by Eleftheria Tsakalozou, Ph.D., Considerations and Expectations when Meeting with the FDA under the Industry Meeting Pilot MIE program, 1/18/2024

Submit An MIE Meeting Request

- Submit one single “Request for MIE” along with the complete meeting package to FDA at MIE@fda.hhs.gov.
- ***Subject Line:*** Request for MIE Pilot Program Meeting
- A confirmation of meeting submission receipt by FDA will be sent via email and will indicate FDA received date

Challenge Question #1

Which of the following scenarios may be granted as an MIE Pilot Meeting:

A. Innovative MIE-focused approaches for BE establishment

B. Non-complex products with complex modeling approaches

C. Novel data analytics tools and approaches for BE establishment and assessment

D. All of the above

Challenge Question #2

Which of the following statements is NOT true?

A. Within 14 days of the meeting package receipt date, FDA will strive to evaluate and assess the meeting package submission. FDA, at its sole discretion, will determine if the MIE meeting request will be granted or denied.

B. The MIE Pilot Meeting is part of GDUFA meetings and will follow GDFUA meeting process and timeline.

C. During the initial assessment of the MIE meeting package, FDA may determine to schedule and host an optional orientation meeting (via videoconference) with the applicant generally within 30 days of the grant decision date.

D. Regardless if an optional orientation videoconference is scheduled, the applicant will participate in a final meeting via videoconference with FDA.

Take Home Messages

- The pilot program serves as a dedicated regulatory platform for industry to explore the proposed MIE approaches, obtain FDA's advice on their feasibility and advancement, and address relevant scientific and technical questions.
- The MIE pilot program is ongoing to accept more meeting requests so that areas of improvement can be identified to support future recommendations.
- We highly encourage applicants to participate
  - Engage with the FDA early in your product development program

Resources

- General Principles Pilot Program: Model-Integrated Evidence (MIE) Industry Meeting Pilot Between FDA and Generic Drug Applicants
- SBIA Workshop: A Deep Dive: FDA's Model-Integrated Evidence (MIE) Industry Meeting Pilot Program for Generic Drugs, January 18, 2024

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Questions?

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Questions about the program may be directed to MIE@fda.hhs.gov

Closing Thought

FDA has been openly encouraging the use of quantitative methods and modeling approaches with MIE to support the development and approval of generic drug products.

Consider the Industry Meeting Pilot MIE program when requesting a meeting with the FDA


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