Model-Integrated Evidence (MIE) Industry Meeting Pilot Program for Generic Drugs: Introduction

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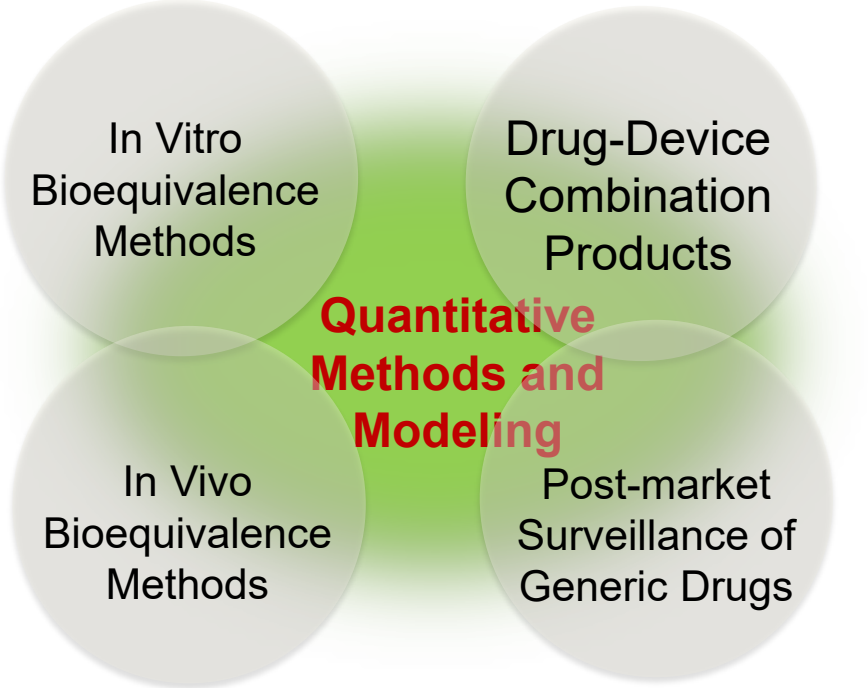
Office of Generic Drugs (OGD)| CDER | US FDA

MIE Industry Meeting Pilot Program for Generic Drugs Webinar
January 18, 2024

Quantitative Methods & Modeling (QMM) for Generic Drug Development and Approval



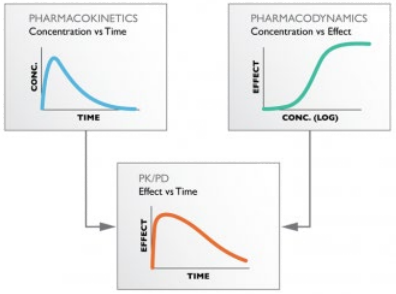
Model-integrated evidence (MIE) refers to using model generated information such as the virtual bioequivalence (VBE) study results not just to plan a pivotal study but to serve as critical evidence

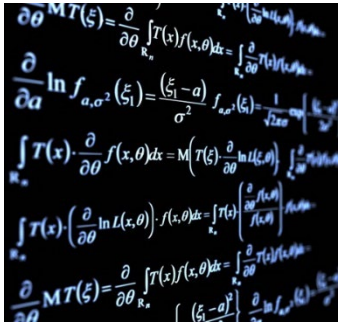
Clin Pharmacol Ther. 2019 Feb;105(2):338-349

Quantitative Methods and Modeling in Office of Generic Drugs

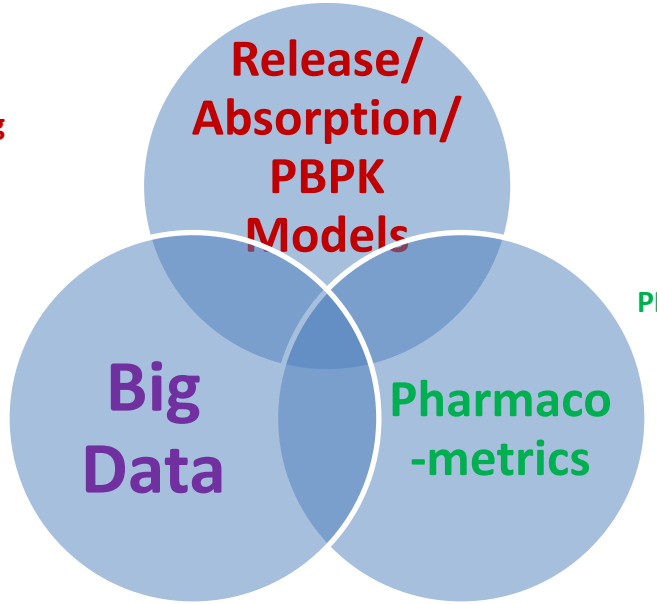
Non-Oral Drug

Oral Drug

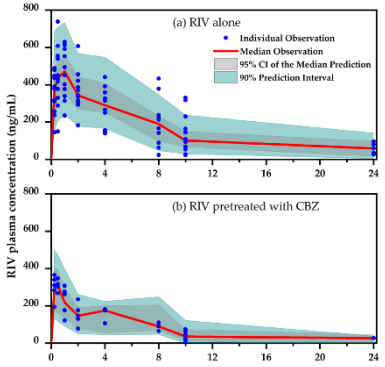




Machine learning toolsets
Analytics for complex mixtures
Systems pharmacology
Risk-based models
Business process models



PK-PD model



Population based model

www.fda.gov

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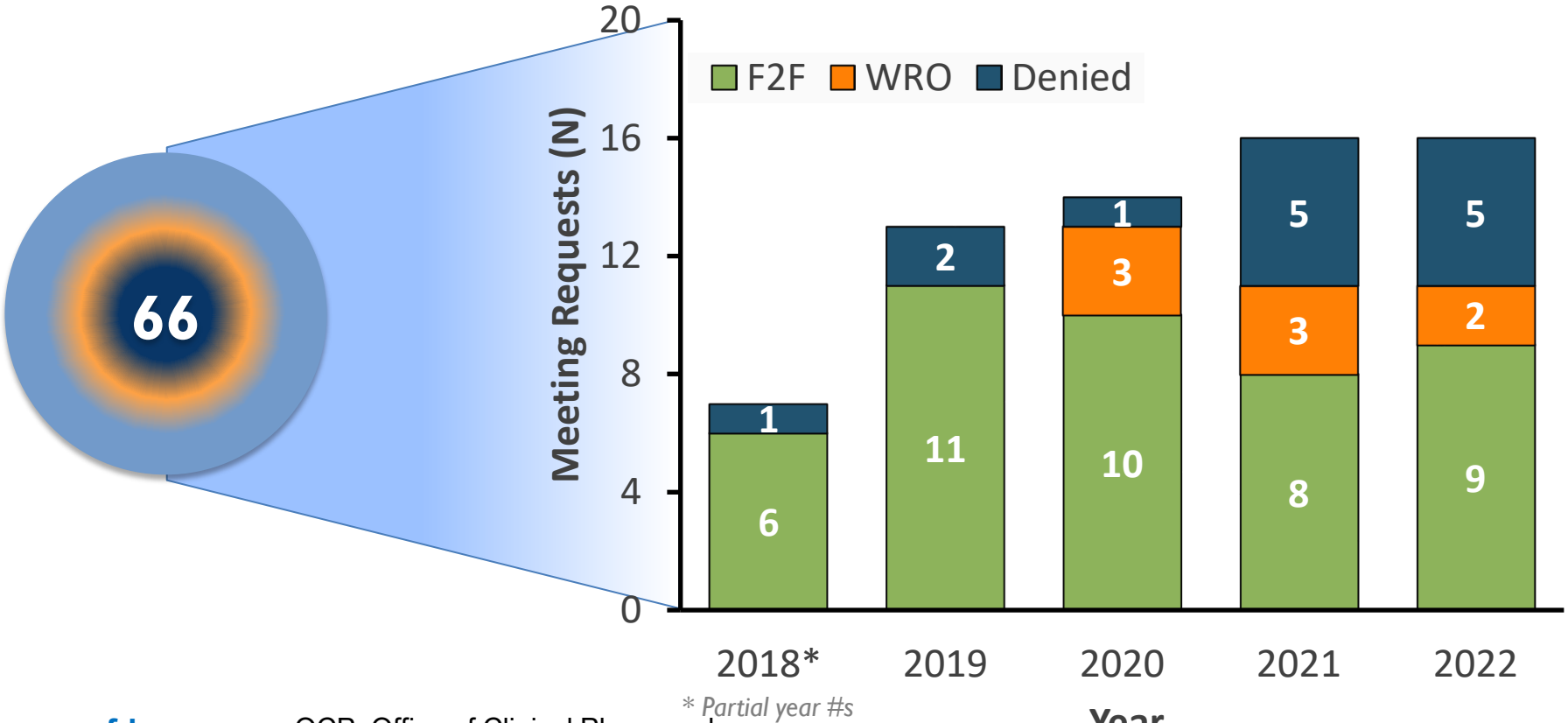
CDER/OCP MIDD Pilot Program Experience



* *Partial year #s*

¤ *Conducted as of Dec 31, 2022*

OCP: Office of Clinical Pharmaoclogy
MIDD: Model Informed Drug Development

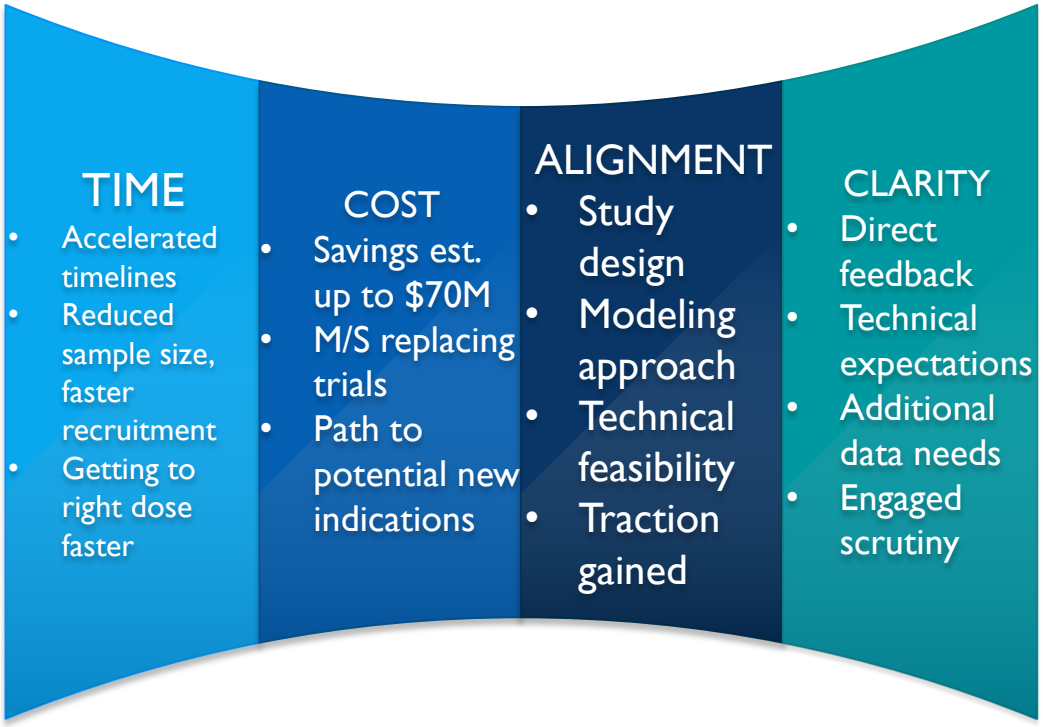
Slide Courtesy: Rajanikanth (Raj) Madabushi

MIDD Pilot Program Impact

Industrial Benefit

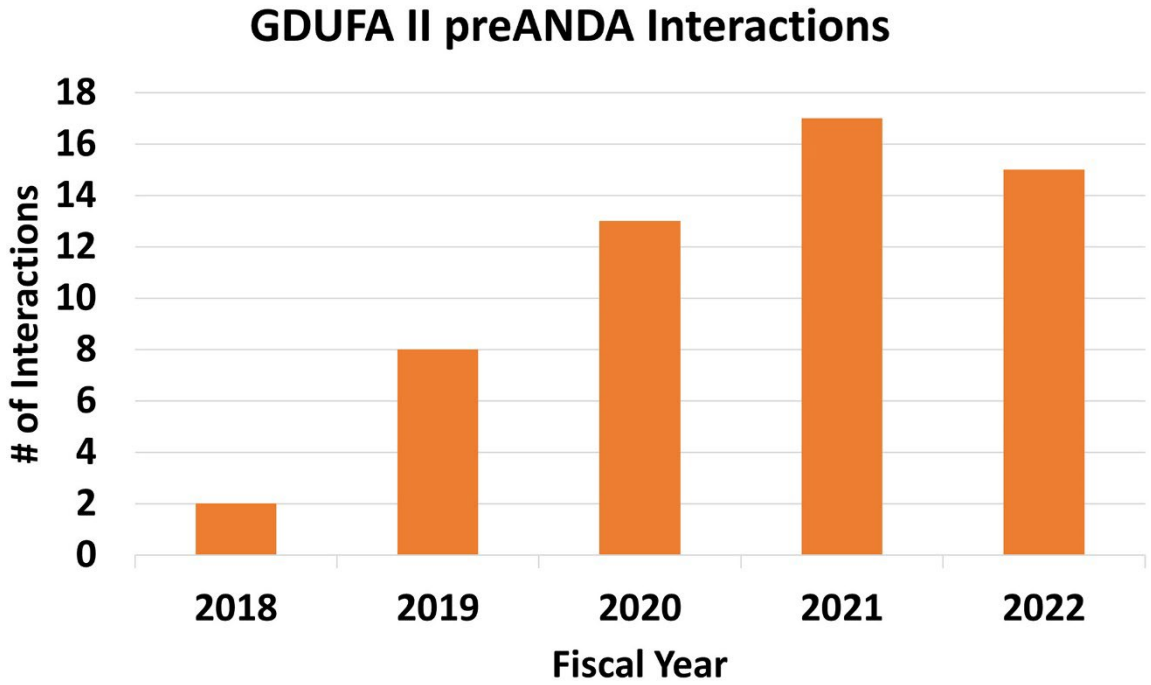
Industrial Perspective on the Benefits Realized From the FDA's Model-Informed Drug Development Paired Meeting Pilot Program

Gerald R. Galluppi[1,*], Satjit Brar[2], Luzelena Caro[3], Yuan Chen[4], Nicolas Frey[5], Hans Peter Grimm[5], Deanne Jackson Rudd[3], Chi-Chung Li[6], Mindy Magee[7], Arnab Mukherjee[8], Lee Nagao[9], Vivek S. Purohit[10], Amit Roy[11], Ahmed Hamed Salem[12,13], Vikram Sinha[3,†], Ahmed A. Suleiman[14], Kunal S. Taskar[15], Vijay V. Upreti[16], Benjamin Weber[17] and Jack Cook[18,*]



Source: Results from International Consortium for Innovation and Quality in Pharmaceutical Development survey
Clin Pharmacol Ther 2021;110(5):1172-1175

Number of pre-ANDA Interactions with Industry Proposed MIE during GDUFA II



Yoon M, et al. CPT Pharmacometrics Syst Pharmacol. 2023 May;12(5):552-555. doi: 10.1002/psp4.12930

Post FDA/CRCG Workshop Survey

- On October 27 and 28, 2022, the U.S. Food and Drug Administration (FDA) and the Center for Research on Complex Generics (CRCG) cosponsored a live virtual workshop titled “Utilizing Modeling Approaches to Support Generic Product Development.”

- More than 1,750 people registered for the workshop, and approximately 820 people attended these sessions on the day of the workshop. The workshop audience had highly diverse backgrounds, including drug product development, clinical study, and regulatory affairs

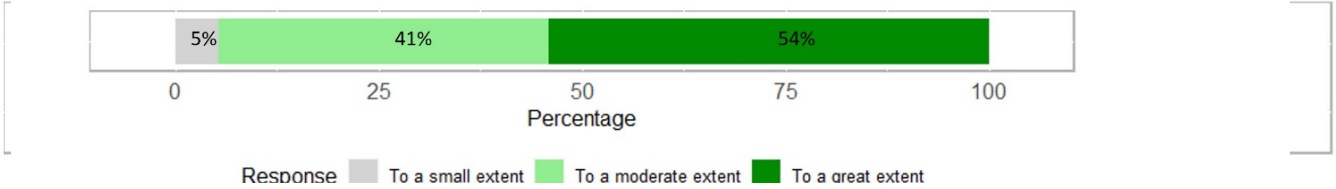
- Post workshop survey was conducted regarding using MIE for generic drug application

Survey Results

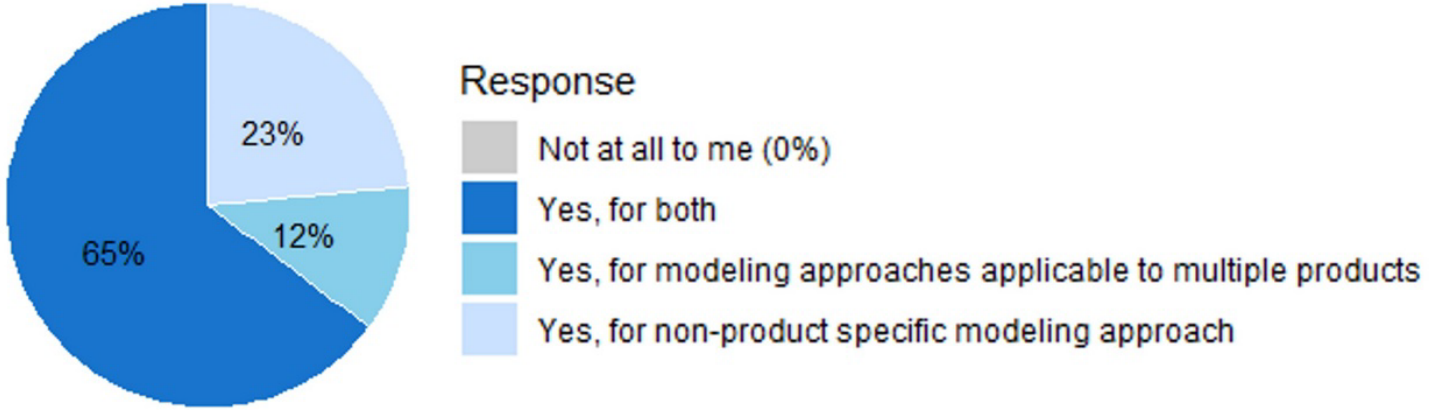
How valuable did you find the content in the presentations during the workshop?

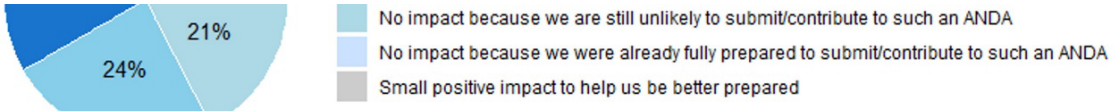
How valuable did you find the content in the panel discussions during the workshop?

A. Did the workshop directly address issues or challenges you face related to model-integrated BE approaches to support generic product development?



How valuable would you find a communication channel with the FDA to discuss modeling approaches relevant to the use of the same model or modeling strategy across multiple submissions for complex drug products?





MIE Pilot

- **Launch Date:** October 1st, 2023
- **Mission:**

  This new pilot program is to provide industry with meetings and opportunities for early interaction for science-driven topics using model-integrated evidence (MIE) approaches for bioequivalence (BE) establishment to facilitate generic drug development and regulatory decision making.
- **Vision:**

  The pilot program allows enhanced scientific communications between generic drug developers and FDA on using 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.

  Specifically, the pilot MIE meeting(s) will focus on discussing scientific and technical topics of using MIE strategies for BE establishment (e.g., feasibility, details in model building, and/or model verification and validation data) while pre-ANDA meetings will be focused on more general scientific and regulatory issue(s).

General Principles Document: https://www.fda.gov/media/172028/download?attachment

Eligibility Criteria for MIE-Pilot

- MIE-focused approaches that are innovative in nature for BE establishment and are not eligible or cannot sufficiently addressed under the existing pre-ANDA and ANDA scientific meeting program to address complex issues pertinent to a single product or multiple products (e.g., common strategies for validating a computational fluid dynamics (CFD) model/platform towards predicting regional deposition of inhaled aerosols from a variety of OIDPs).
- Non-complex Products with complex modeling approaches supporting BCS-based biowaivers and other BE study waivers that are outside current recommendations.
- Novel data analytics tools such as modeling methodology advancement or new applications of a modeling approach, e.g., equivalence analysis of complex particle size distribution (PSD), new quantitative approaches for sameness assessment, and application of novel data analytics approaches (e.g., machine learning methodology) for equivalence assessment.

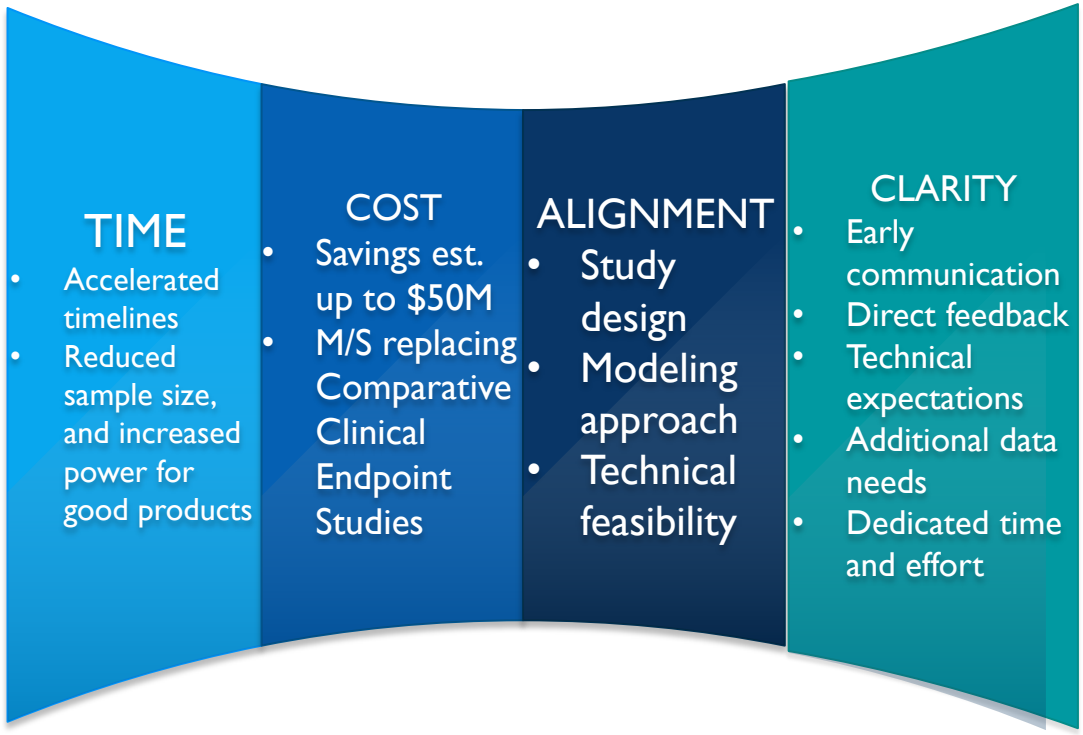
Key Operational Aspects

- Post its launch on October 1st, 2023 and FDA will evaluate the pilot program at the end of year one or after five meetings have been held, whichever occurs first to determine the next phase of the pilot program
- Areas of Focus
  - Locally acting products (e.g., orally inhaled and topical dermatological products), and long-acting injectables etc.

  - Non-complex products: Novel biowaiver requests supported by mechanistic modeling, and oncology products

Impacts and Benefits

Industrial Benefit →



Agency Benefit ↓

- Efficiency to handle multiple products
- Reducing number of cycles for drug approval
- Eco-system with industry to develop effective BE approaches

Slide Courtesy: Modified from Kim Bergman & Issam Zineh

Today's Agenda

Opening Remarks (15 min)	**Introduction to MIE Industry Meeting Pilot Program** Liang Zhao, PhD *Director* Division of Quantitative Methods and Modeling (DQMM) | Office of Research and Standards (ORS) Office of Generic Drugs (OGD) | CDER	1:05 - 1:20 pm
Talk 1 (15 min)	**MIE Pilot Program: Process Overview** Maria Monroy-Osorio *Regulatory Health Project Manager*, ORS|OGD|CDER	1:20 - 2:35 pm
Talk 2 (15 min)	**Potential Topics for Discussion Through the MIE Industry Meeting Pilot Program** Andrew Babiskin, PhD *Lead Pharmacokineticist*, DQMM | ORS | OGD | CDER	1:35 - 1:50 pm
Talk 3 (15 min)	**Considerations and expectations when meeting with the FDA under the Industry Meeting Pilot MIE program** Eleftheria Tsakalozou, PhD *Senior Pharmacologist (Acting TL),* DQMM | ORS | OGD | CDER	1:50 – 2:05 pm
Panel Discussion (20 min)	**Moderator:** Lanyan (Lucy) Fang, PhD, *Deputy Director*, DQMM | ORS | OGD| CDER **Panelists:** • Bhagwant Rege, PhD, *Division Director*, Division of Biopharmaceutics (DB) | Office of New Drug Products (ONDP) | Office of Pharmaceutical Quality (OPQ) | CDER • Partha Roy, PhD, *Director,* Office of Bioequivalence (OB) | OGD | CDER • Robert Lionberger, PhD, Director, ORS|OGD|CDER • Liang Zhao	2:05 - 2:25 pm
Speaker Q&A Discussion (30 min)	**Moderator:** Forest "Ray" Ford, Jr. **Panelists:** • Liang Zhao • Eleftheria Tsakalozou • Andrew Babiskin • Maria Monroy-Osorio • Fang Wu, PhD, *Senior Pharmacologist*, DQMM | ORS | OGD | CDER • Meng Hu, PhD, *Lead Engineer*, DQMM | ORS | OGD | CDER	2:25 - 2:55 pm
Closing Remarks (5 min)	**Closing Remarks** Robert Lionberger or Lei Zhang	2:55 - 3:00 pm

Acknowledgment

- MIE-Pilot WG including Colleagues from
  - ORS/OGD
  - OB/OGD
  - Comm Staff and OGDP/OGD
  - OCP/OTS
  - OPQ

- ORS and OB leadership
  - Robert Lionberger
    Lei Zhang
  - Partha Roy
- All other stakeholders