MIDD Paired Meeting Program:
An Update

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Office of Translational Sciences
U.S. Food and Drug Administration

Outline

- Background
- MIDD Paired Meeting Pilot Program
- PDUFA 7 & MIDD Paired Meeting Program

Model-informed Drug Development (MIDD)

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

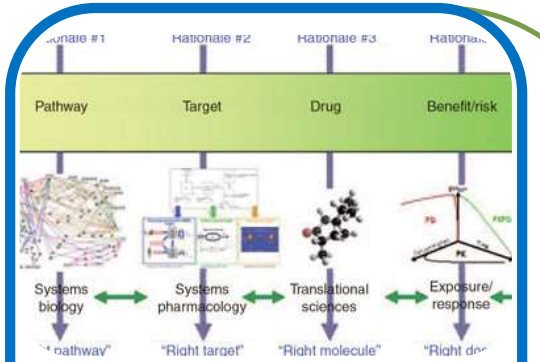
* From PDUFA 6; Excludes statistical designs involving complex adaptations, Bayesian methods, or other features requiring computer simulations to determine the operating characteristics of a confirmatory clinical trial.

Huang SM 2019 AAPS

PDUFA 6: Regulatory Decision Tools

Patient Voice

Complex Innovative Trial Designs



Model-Informed Drug Development

Analysis Data Standards

Benefit/Risk Assessment

Biomarker Qualification

Advancing MIDD under PDUFA VI

A Holistic and Integrative Approach

U.S. FOOD & DRUG ADMINISTRATION

Madabushi 2019 [PMID 31081932]

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

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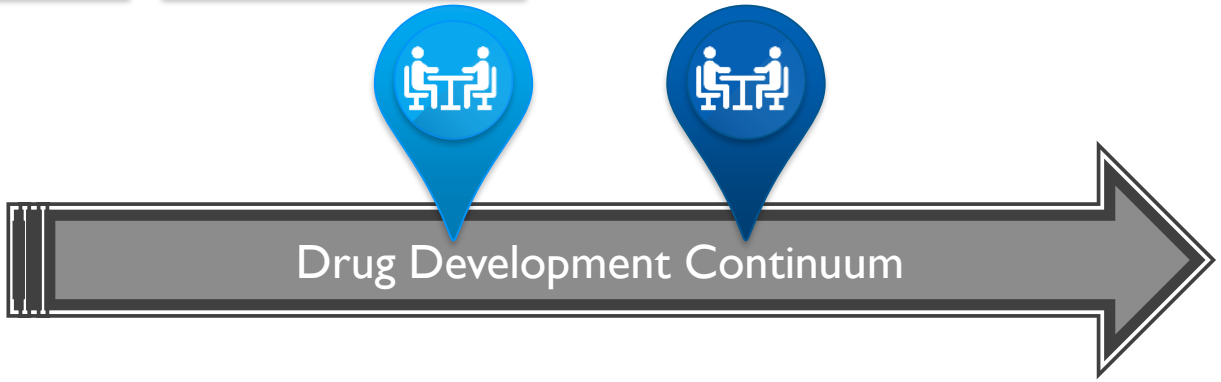
MIDD Paired Meeting Pilot Program

A dedicated forum for regulatory interaction on MIDD applications in specific drug development programs

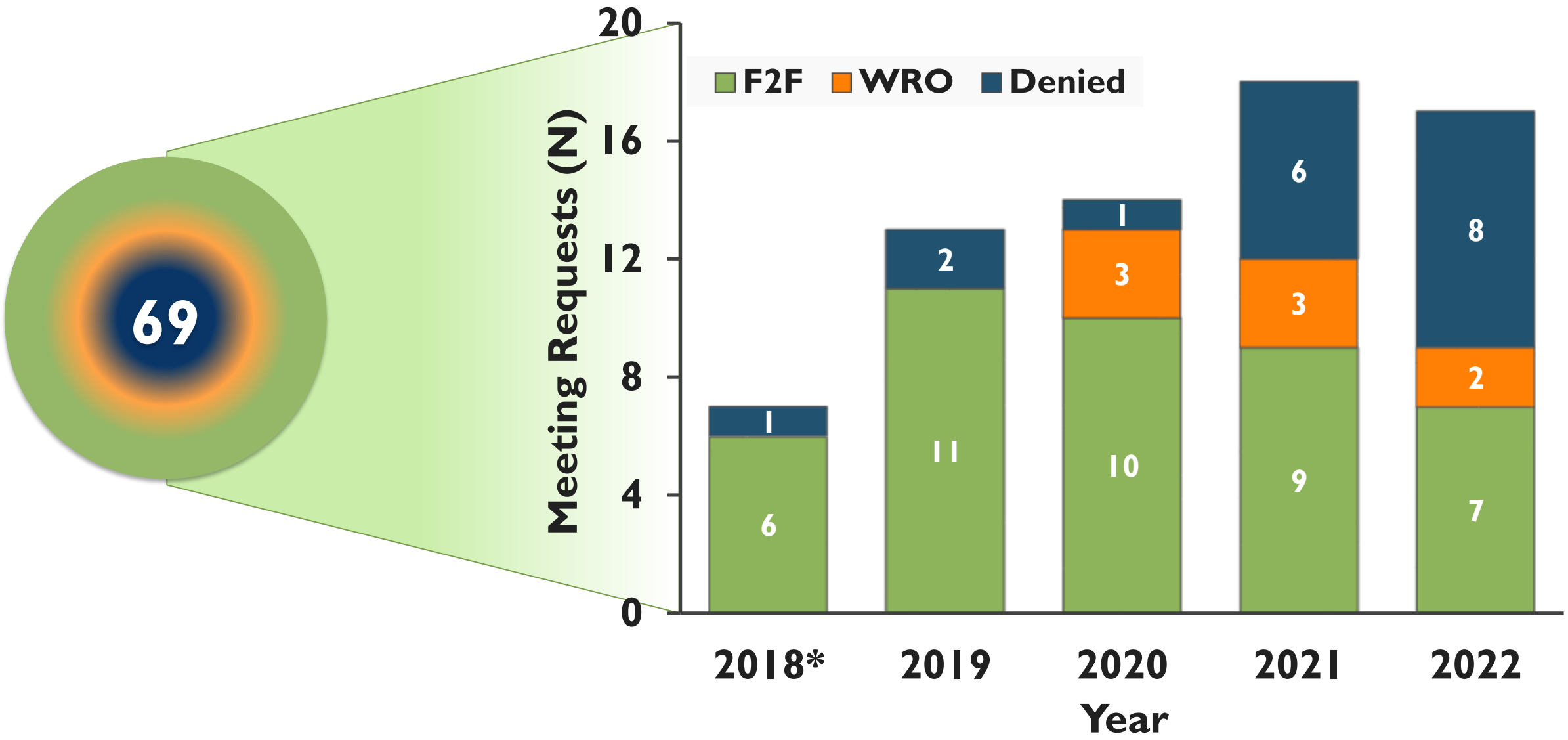
Dose Section and Optimization

Clinical Trial Simulation

Mechanistic Safety Evaluation



CDER/OCP Pilot Program Experience



* *Partial year #s*

¤ *Conducted as of Dec 31, 2022*

CDER/OCP Program Experience

	2018	2019	2020	2021	2022	Total
Sponsor meetings	7	15	14	11	12	59
Internal meetings	14	36	37	25	31	143
Written Response Only	-	1	4	6	2	13

THERAPEUTIC AREAS

	2018	2019	2020	2021	2022
Oncology	●	●	●	●	●
Cardiology	●	●		●	●
Dermatology	●	●			
Immunology/ Inflammation	●	●		●	●
Infectious Disease	●		●	●	●
Non-Malignant Hematology		●	●	●	●
Neurology		●	●	●	
Pulmonary		●	●		
Endocrinology			●	●	●
Gastroenterology			●		
Nephrology			●	●	●
Ophthalmology			●	●	
Psychiatry				●	●
Hepatology				●	

Applicable across wide spectrum of therapeutic areas

Resource intensive and involves engagement of multidisciplinary stakeholders

Flexibility, transparency, and clarity in feedback

Office of Clinical Pharmacology – 2022 Annual Report https://www.fda.gov/media/164793/download

CDER/OCP Pilot Program Impact

Targeted Applications to Advance Drug Development & Review

U.S. FOOD & DRUG ADMINISTRATION

Drug Development

Model validation & clinical trial simulation to inform trial design and patient selection

Strategies for dose selection, optimization and risk mitigation

Alternative approaches for therapeutic individualization

Regulatory pathway seeking approval of new dose, dosing regimen, formulation, etc.

Regulatory Approvals

- **Ramucirumab**

  Approval of shorter infusion option

- **Sotalol Hydrochloride**

  Approval of a new dosing strategy that reduces the hospital stay from 3 days to 1day

- **Cetuximab**

  Approval of a dosing regimen with extended inter-dosing interval

- **Valbenazine**

  Approval of a new dose option as part of titration

Full prescribing information is available at:

Ramucirumab: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/125477s036lbl.pdf
Sotalol Hydrochloride: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/022306s005lblrpl.pdf
Cetuximab: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125084s277s280lbl.pdf
Valbenazine: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/209241s020lbl.pdf

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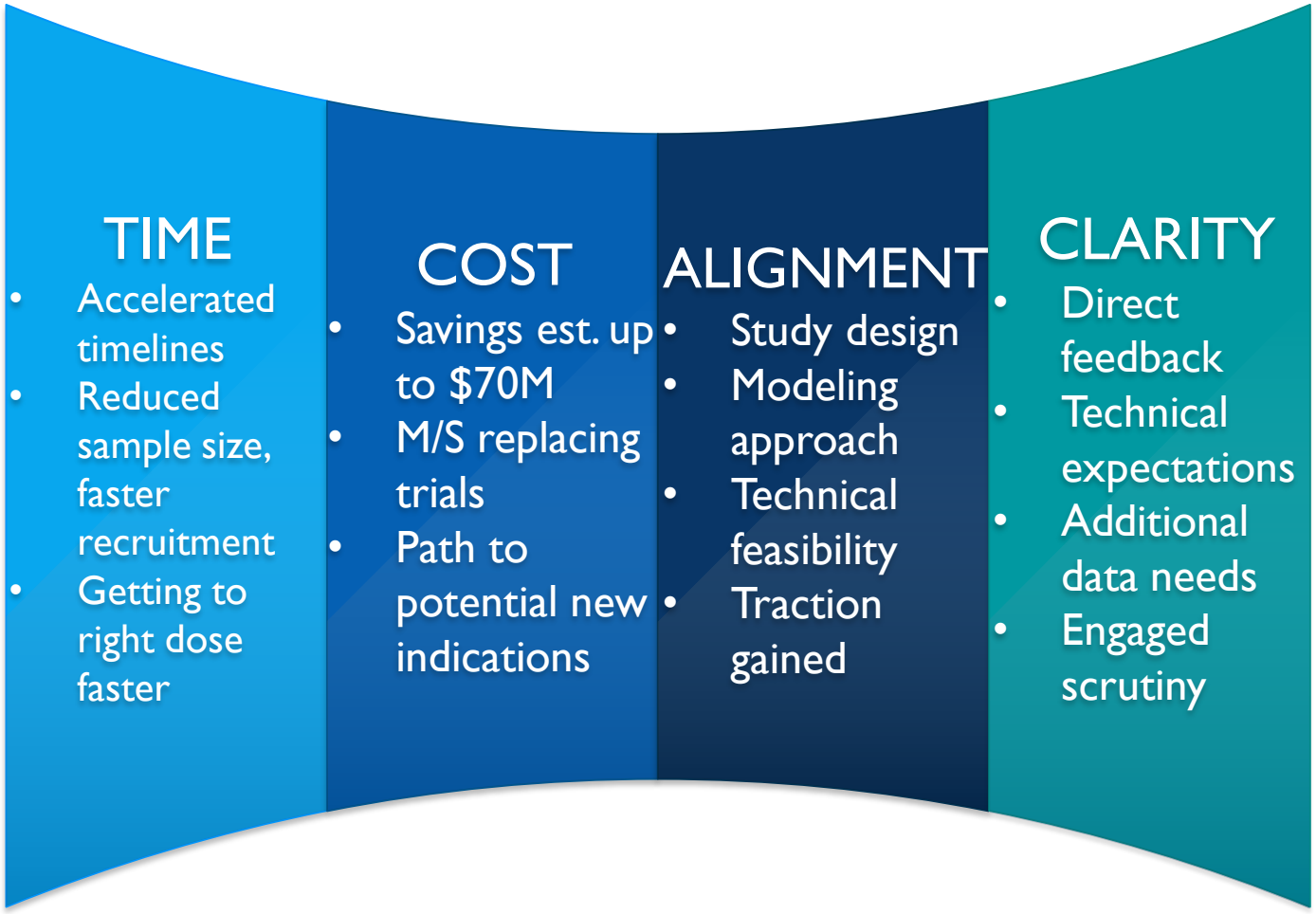
Pilot Program Impact

Industrial Benefit



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

Slide Courtesy: Kim Bergman & Issam Zineh

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MIDD under PDUFA 7

FDA will build on the success of the "model-informed drug development" (MIDD) approaches by continuing to advance and integrate the development and application of exposure-based, biological, and statistical models derived from preclinical and clinical data sources in drug development and regulatory review.

By no later than the end of 1st Quarter of FY 2023, FDA will publish a Federal Register Notice announcing the **continuation of the MIDD paired meeting program**, outlining program eligibility, and describing the proposal submission and selection process.

FDA will issue a **Request for Information (RFI)** to elicit public input for identifying **priority focus areas for future policy or guidance development and stakeholder engagement.** This RFI will be issued by no later than the end of FY 2024.

PDUFA REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES FISCAL YEARS 2023 THROUGH 2027

NATIONAL ARCHIVES
FEDERAL REGISTER
The Daily Journal of the United States Government

FDA U.S. FOOD & DRUG ADMINISTRATION

Notice

Prescription Drug User Fee Act of 2023 VII Meetings Program for Model-Informed Drug Development Approaches

A Notice by the Food and Drug Administration on 01/11/2023

Comments on this document are being accepted at Regulations.gov.

SUBMIT A FORMAL COMMENT

Read the 1 public comment

PUBLISHED DOCUMENT

AGENCY:

Food and Drug Administration, HHS.

ACTION:

Notice.

SUMMARY:

The seventh iteration of the Prescription Drug User Fee Act (PDUFA VII), incorporated as part of the FDA User Fee Reauthorization Act of 2022, highlights the goal of advancing model-informed drug development (MIDD). The Food and

DOCUMENT DETAILS

Printed version:
PDF

Publication Date:
01/11/2023

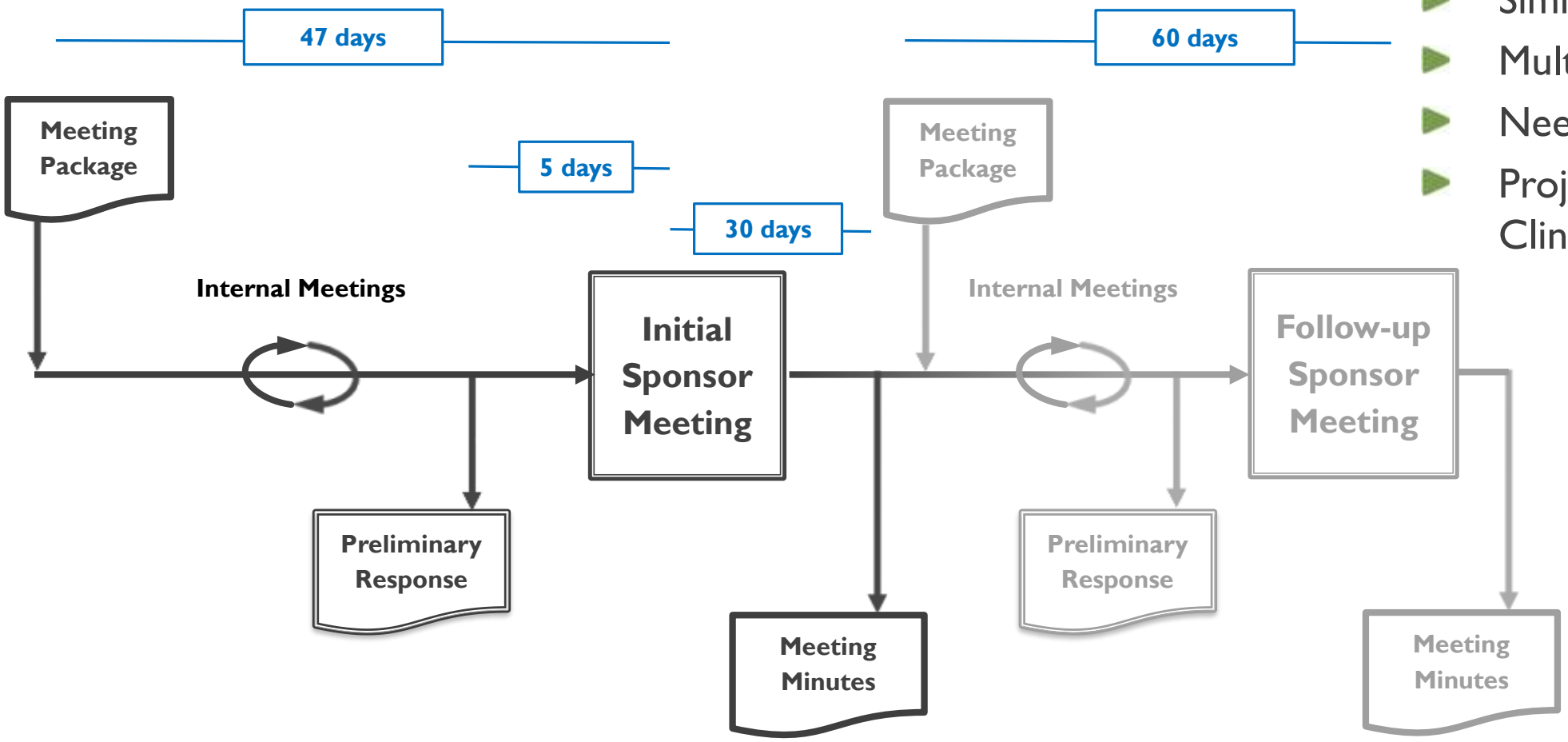
Agencies:
Food and Drug Administration

Dates:
FDA will accept requests to participate in the program on a continuous basis beginning on October 1, 2022, through June 1, 2027. See section III of this notice for instructions about

MIDD Paired Meeting Program

- Not a pilot program anymore!
- Meetings will be granted every quarter
  - FDA MIDD Selection Committee will review the meeting requests and provide recommendations
- Eligibility criteria remains the same
- Topic areas not limited to those initially prioritized under PDUFA 6
- Some changes incorporated based on experience

MIDD Paired Meeting Process

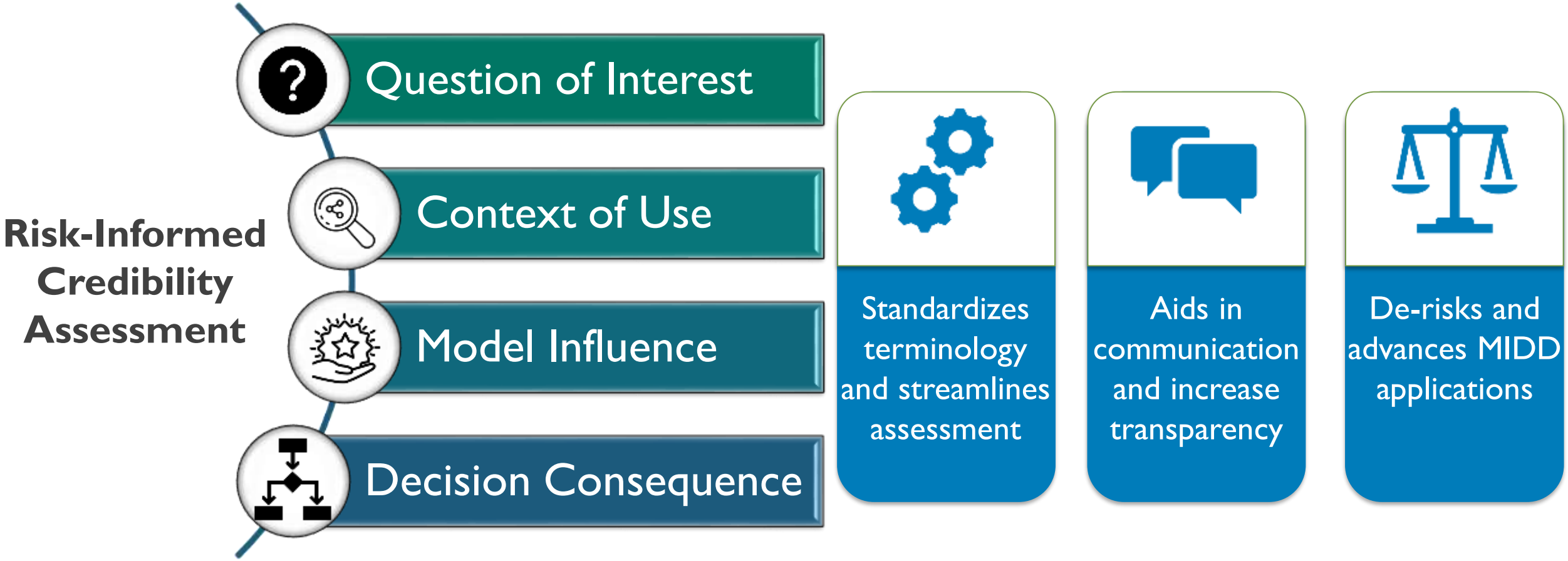


Key Highlights

- Similar to Type C Meetings
- Multidisciplinary
- Need based follow-up
- Project managed by Office of Clinical Pharmacology

MIDD Paired Meeting Program

Content and Format of Meeting Information Package



Kuemmel *et al* 2020 PMID: 31652029; Viceconti *et al* 2020 PMID: 31991193
https://www.fda.gov/drugs/news-events-human-drugs/development-best-practices-physiologically-based-pharmacokinetic-modeling-support-clinical
https://www.fda.gov/drugs/development-resources/model-informed-drug-development-pilot-program
https://www.govinfo.gov/content/pkg/FR-2023-01-11/pdf/2023-00389.pdf

Summary

- The Pilot Program under PDUFA 6 demonstrated tangible benefits to drug development and regulatory decision-making
- PDUFA 7 provides an opportunity to build on the success achieved under PDUFA 6

MIDD Paired Meeting Program – A Multidisciplinary Landscape

The program activities bring together multidisciplinary review staff from across and beyond CDER, including OB, OCP, OMP, OND, OPQ, OSE, OTS, and CBER – OBE.

Acknowledgements

Issam Zineh – Director, Office of Clinical Pharmacology
Jessica Benjamin – Associate Director, Regulatory Affairs
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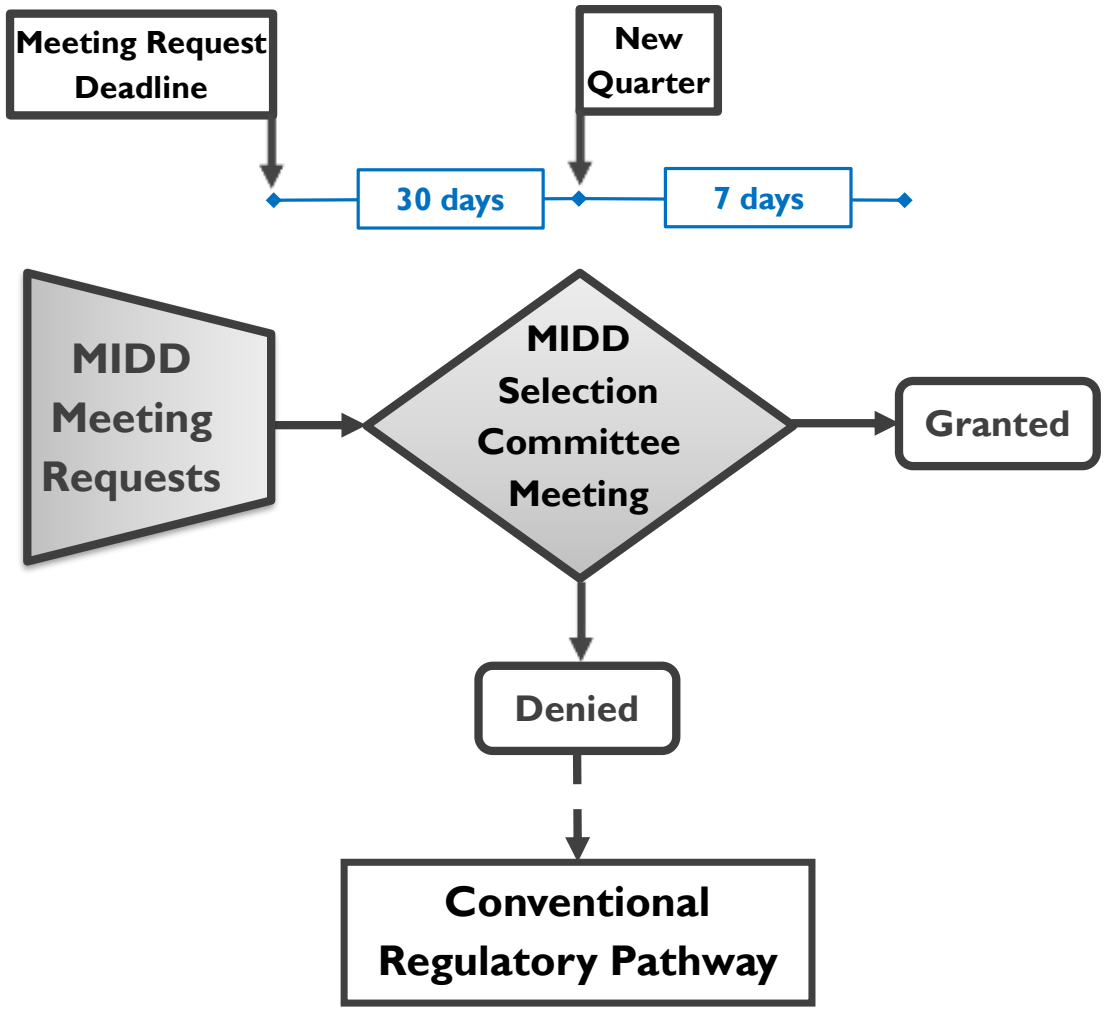
Kunal Naik – Executive Program and Project Management
Hao Zhu– Director, Division of Pharmacometrics
Jeffry Florian – Associate Director, Division of Applied Regulatory Science
Raajan Naik – Policy Analyst, Guidance and Policy Team
MIDD Steering Committee, MIDD Selection Committee
Pilot Program Participants

BACKUP

Selection Process



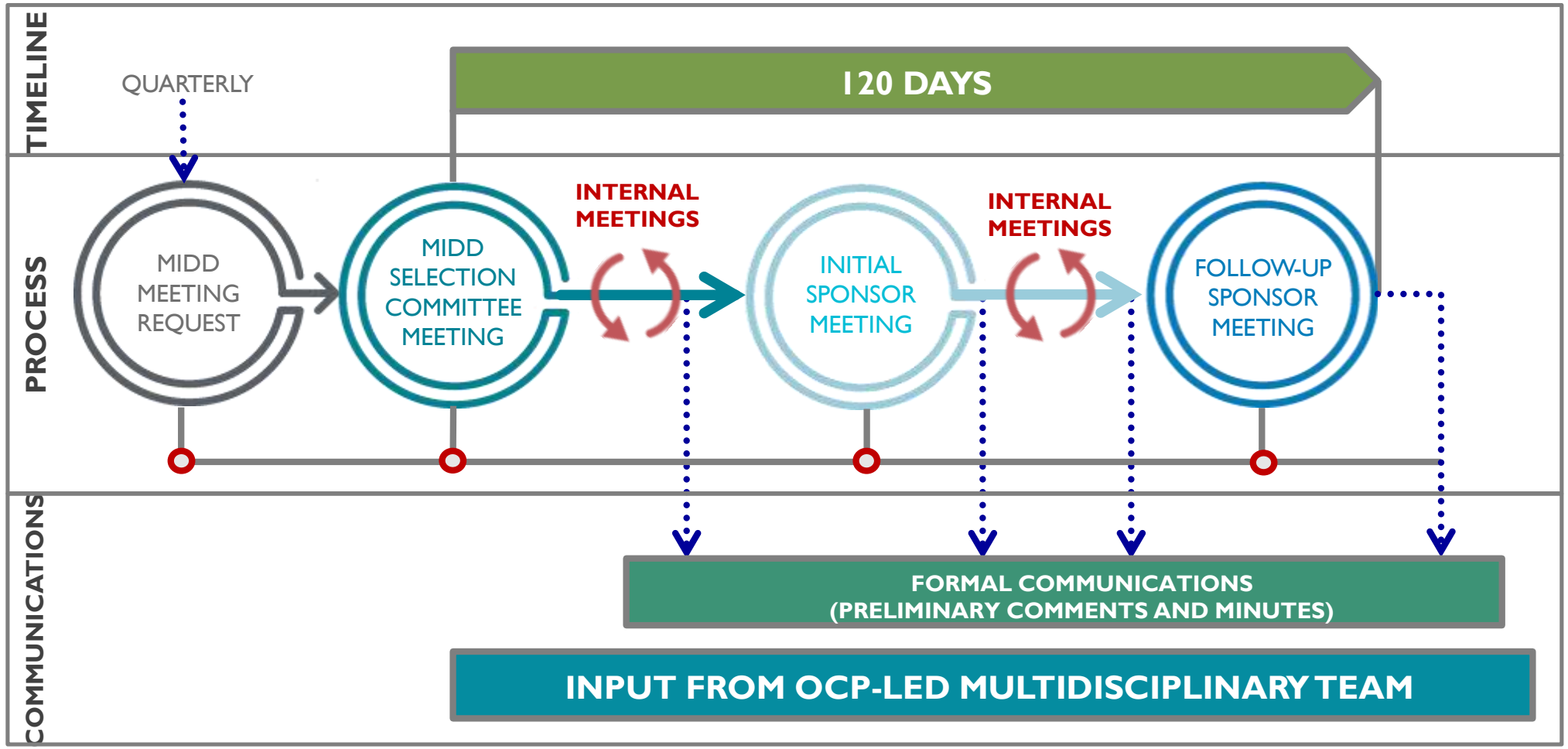
FDA MIDD Selection Committee

- Office of Clinical Pharmacology — CDER
- Office of Biostatistics — CDER
- Office of New Drugs — CDER
- Office of Regulatory Policy — CBER
- Office of Biostatistics and Epidemiology — CBER
- Office of Tissue and Advanced Therapies — CBER
- Office of Vaccines Research and Review — CBER

Selection Criteria

- Acceptability of the MIDD approach
- Expertise and familiarity
- Novelty of the application
- Potential impact

MIDD Pilot Program Process



Courtesy: Kimberly Bergman