FDA Workshop

Streamlining Drug Development and Improving Public Health through Quantitative Medicine

APRIL 25, 2024

Disclaimer

The views presented in this workshop represent the personal opinions of the individual speakers and do not reflect the official positions of the United States Food and Drug Administration (FDA).

Workshop Logistics

- During the workshop - Please use the Q&A for any questions
- After the workshop - The slides and recording will be distributed and available on the workshop webpage.
  - https://www.fda.gov/drugs/news-events-human-drugs/streamlining-drug-development-and-improving-public-health-through-quantitative-medicine-introduction
- Other inquiries - CDERQuantMed@fda.hhs.gov

Opening Remarks

Patrizia Cavazzoni, MD,

Director of the Center for Drug Evaluation and Research (CDER)

An Introduction to the CDER Quantitative Medicine Center of Excellence (QM CoE)

Rajanikanth (Raj) Madabushi
Director, CDER Quantitative Medicine Center of Excellence

FDA CDER Virtual Workshop: Streamlining Drug Development and Improving Public Health through Quantitative Medicine (April 25, 2024)

Quantitative Medicine (QM)

The development and application of exposure-based, biological, and quantitative modeling and simulation approaches derived from nonclinical, clinical, and real-world sources to inform drug development, regulatory decision-making, and patient care.

- Streamline and accelerate drug development throughout the product lifecycle
- Identify, quantify, and address uncertainty earlier in the lifecycle
- Contribute to the totality of understanding of a drug's benefits and risks.

QM at CDER

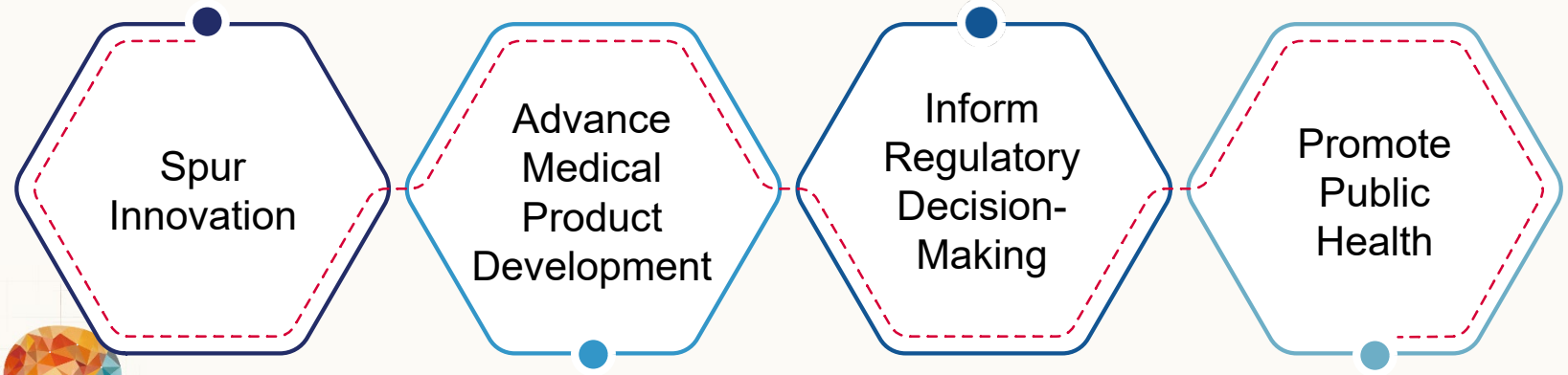
CDER has been at the forefront of advancing QM to inform pre-market product review, post-market product assessment, policy development, and policy implementation.

- Model-informed drug development (MIDD)
- Complex innovative trial design (CID)
- Fit-for-purpose initiative (FFP)
- Model integrated evidence (MIE)
- Physiology based biopharmaceutics modeling (PBBM)

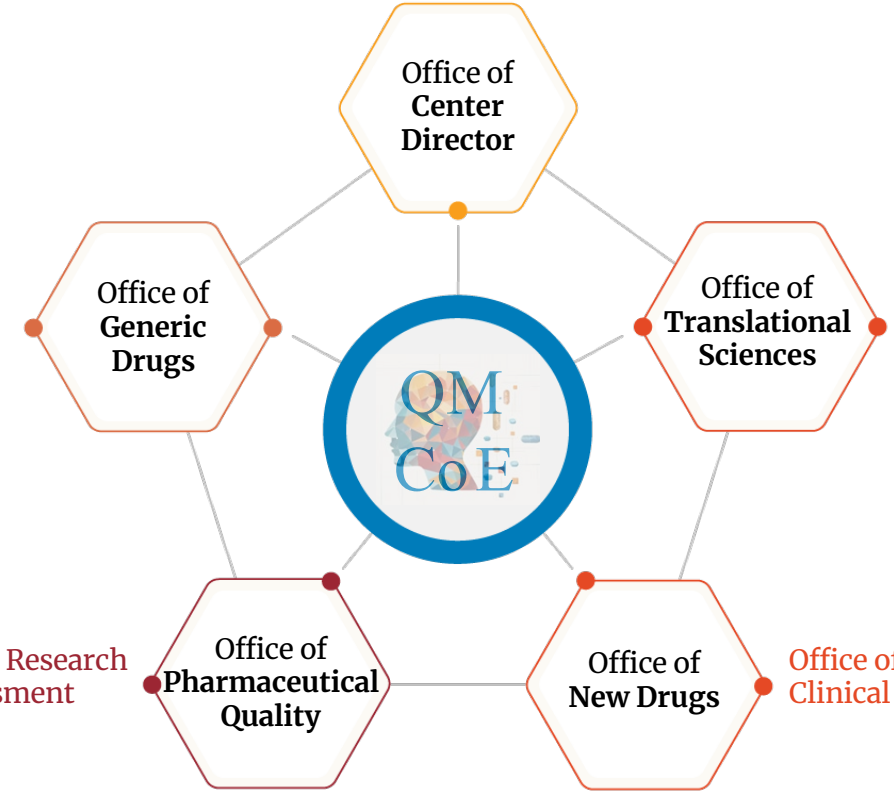
Opportunity to maximize synergies across CDER by centrally coordinating efforts

CDER QM Center of Excellence

A CDER-wide enterprise that will facilitate the continuous evolution and consistent application of QM for drug development and regulatory decision-making.



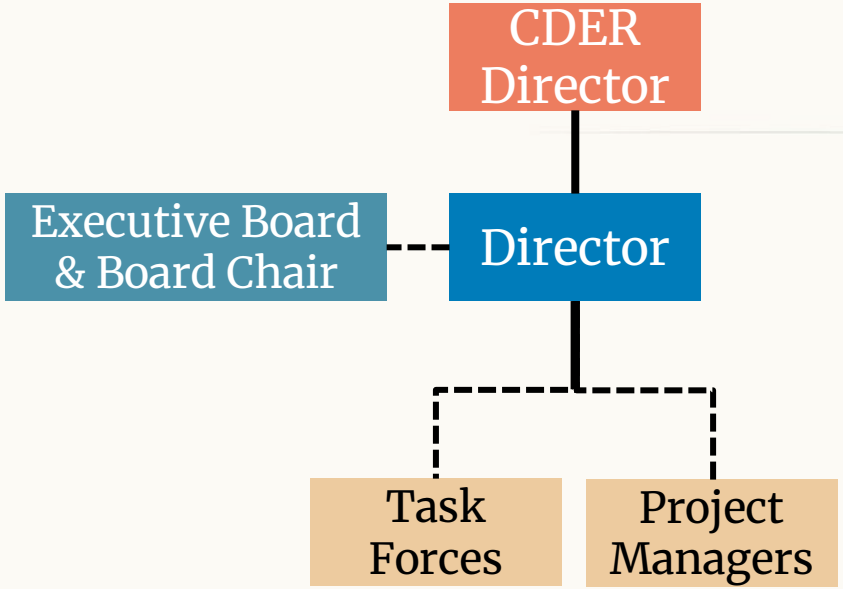
CDER QM CoE Participating Offices



CDER QM CoE Governance

Key features

- ✓ Fosters collaboration and connectivity across key stakeholders in CDER
- ✓ Ensures clarity of roles, responsibilities, and accountability
- ✗ Not an organizational realignment



CDER QMCoE Leadership

Executive Sponsor: Patrizia Cavazzoni, MD
QM CoE Director: Raj Madabushi, PhD
Board Chair: Issam Zineh, PharmD, MPH, FCP, FCCP
Board Project Manager: Daphne Guinn, PhD
Board Members:

Robert Lionberger, Office of Research and Standards, Office of Generic Drugs
Liang Zhao, PhD, Division of Quantitative Methods & Modeling (DQMM), Office of Research and Standards, Office of Generic Drugs

Thomas O'Connor, Office of Pharmaceutical Quality Research, Office of Pharmaceutical Quality
Bhagwant Rege, Office of Product Quality Assessment I, Office of Pharmaceutical Quality

Stella Grosser, Division of Biometrics VIII, Office of Biostatistics, Office of Translational Sciences
Lei Nie, Ph.D., Division of Biometrics IV, Office of Biostatistics, Office of Translational Sciences

Hao Zhu, Division of Pharmacometrics, Office of Clinical Pharmacology, Office of Translational Sciences
Qi Liu, Office of Clinical Pharmacology, Office of Translational Sciences

James Smith, Office of New Drug Policy, Office of New Drugs
Nikolay Nikolov, Office of Immunology and Inflammation (OII), Office of New Drugs

Quantitative Medicine Center of Excellence

SCOPE & FOCUS

CDER QM CoE Scope

Quantitative Medicine Center of Excellence

- Pharmaco-statistical models
- Mechanistic modeling
- Machine learning and artificial intelligence
- Biomarker-endpoint development
- Clinical trial simulations and in silico predictions

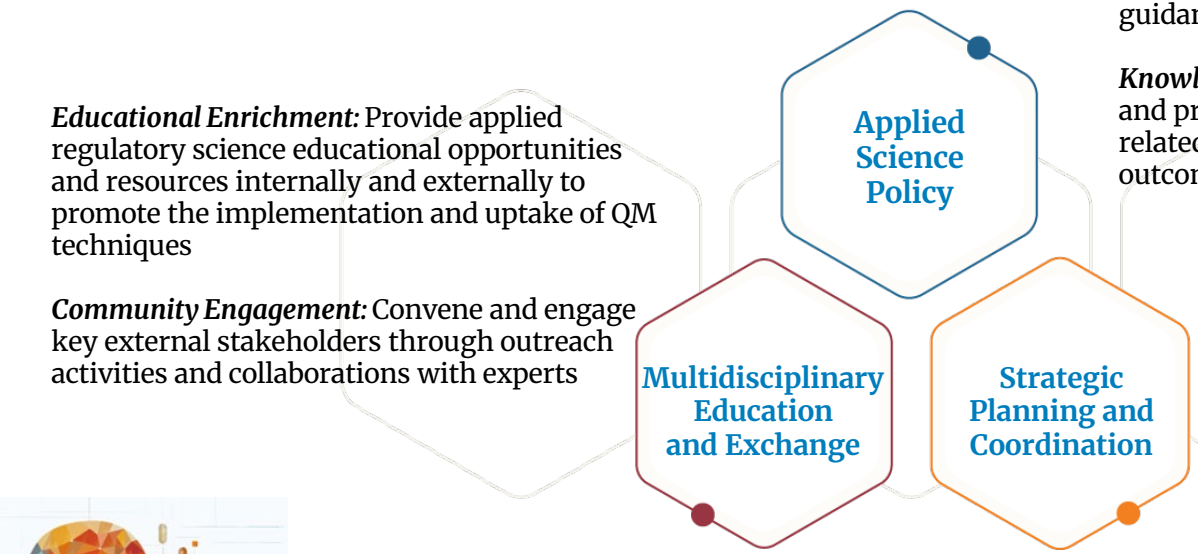
CDER QM CoE Focus

Policy Development: Lead the development and implementation of evidence-based scientific guidances, policies and best practices

Knowledge Management: Catalog precedents and promote best practices and standards related to QM; document and disseminate outcomes of QM applications

Educational Enrichment: Provide applied regulatory science educational opportunities and resources internally and externally to promote the implementation and uptake of QM techniques

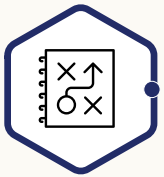
Community Engagement: Convene and engage key external stakeholders through outreach activities and collaborations with experts



Strategic Planning: Identify priorities and determine areas of further research and development in CDER

Coordination: Coordinate and elevate existing QM-related scientific and regulatory initiatives; implement strategic and tactical plans to address CoE goals

Going Forward



Develop Strategic Plan

Create Task Forces

Engage Stakeholders

Share Resources

Together, we can champion, advance, and integrate quantitative medicine for maximizing patient and societal benefit.

CDERQuantMed@fda.hhs.gov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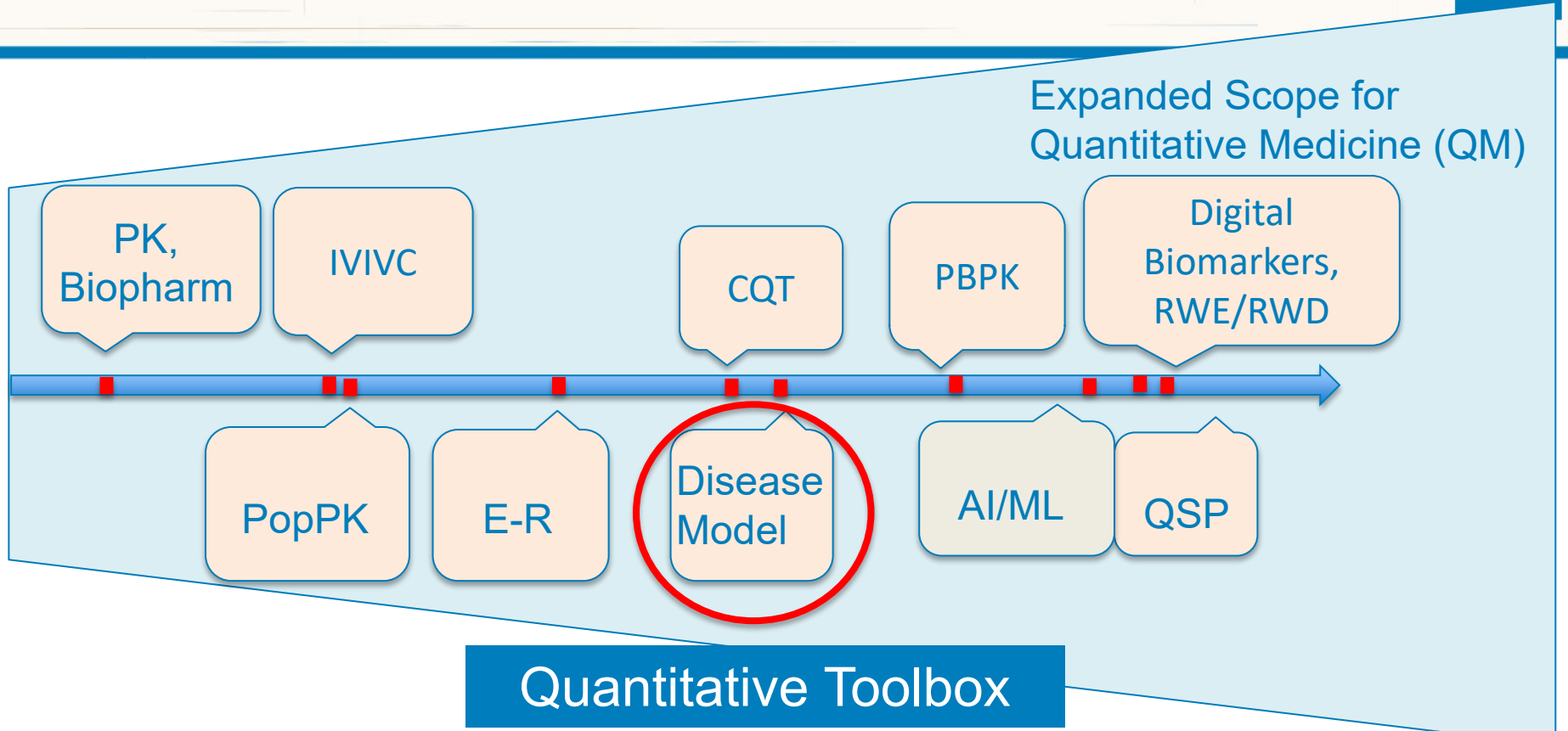
Quantitative Medicine in the Office of Clinical Pharmacology: From the Past to the Future

Hao Zhu, Ph.D., Mstat
Division Director
Division of Pharmacometrics,
FDA/CDER/OTS/OCP

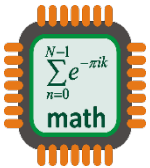
Quantitative Medicine Center of Excellence Workshop
(April 2024)


Quantitative Medicine In OCP
Technical Exploration
Broadened Collaboration
Sponsor Engagement
Policy Development
Skilled Reviewers + Strong Leadership

Technical Exploration



Expanded Scope for QM: Disease Models



No	Disease Model	Use
1	NSCLC Model [1]	Late Phase Trial Design.
2	Parkinson's Disease Model [2]	Endpoint Selection and Clinical Trial Design
3	Alzheimer's Disease Model [3]	Endpoint Selection and Clinical Trial Design
4	Diabetes Disease Model [4]	Clinical Trial Design
5	Huntington's Disease Model [5]	Patient Enrichment, Clinical Trial Design
6	DMD Disease Model [6]	Patient Enrichment, Clinical Trial Design
7	HIV Model [4]	Clinical Trial Design
8	Schizophrenia Model [7]	Pediatrics Extrapolation
9	Bipolar I disorder Model [8]	Pediatrics Extrapolation
10	Weight Loss Model [9]	Clinical Trial Design
11	Bone Density Model [10]	Clinical Trial Design
12	Idiopathic Pulmonary Fibrosis Model [11]	Patient Enrichment, Clinical Trial Design
13	Rheumatoid Arthritis Model [12]	Patient Enrichment, Clinical Trial Design
14	Pulmonary Arterial Hypertension Model [13]	Endpoint Selection and Clinical Trial Design

https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/division-pharmacometrics.

Broadened Collaboration

Internal Collaboration

- CDER
  - OND
  - OB
  - OGD
  - OPQ
- CBER
- CDRH
- OCE

External Collaboration

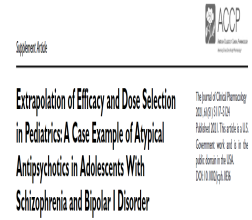
- Academia
- Professional Association
- Global Regulatory Agencies

Joint Efforts:
Reviews, Research Projects, Policy Development, & Outreach

Joint Efforts:
Research Projects, Tool Development, Training Programs, Policy Development, & Outreach

Collaborations for Innovation

• Internal Collaboration


Supplement Article

Extrapolation of Efficacy and Dose Selection in Pediatrics: A Case Example of Atypical Antipsychotics in Adolescents With Schizophrenia and Bipolar I Disorder

Joint research among OND, OCP, and OB to establish pediatric extrapolation, identify novel endpoints, select patients, etc

Pharmacokinetic-Based Criteria for Supporting Alternative Dosing Regimens of Programmed Cell Death Receptor-1 (PD-1) or Programmed Cell Death-Ligand 1 (PD-L1) Blocking Antibodies for Treatment of Patients with Cancer Guidance for Industry

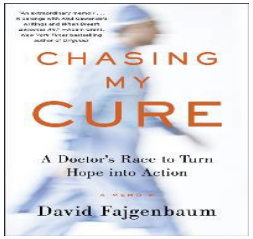
To establish new policy and guidance to streamline new drug development.

CDER Scientific Rounds:

To engage internal stake holders for experience sharing, issue identification and technical discussion

• External Collaboration

Collaboration with Dr. Fajgenbaum at University of Pennsylvania to explore potential biomarkers for Castleman's disease



To achieve global harmonization on Model Informed Drug Development (ICH M15 MIDD guideline)

To establish technical standard.
To enhance experience sharing
To engage broad discussion on issues

ISoP
INTERNATIONAL SOCIETY OF PHARMACOMETRICS

Sponsor Engagement

• MIDD Paired Meeting Program

Jointly administered by CDER and CBER for IND, NDA, and BLA holders to support the use of innovative modeling tools in a specific development program.

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

*: Model-Informed Drug Development Paired Meeting Program | FDA

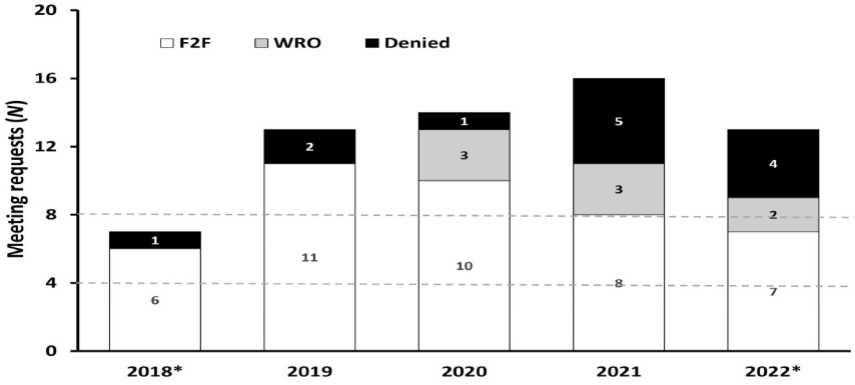
• FFP Program

The Fit-for-Purpose (FFP) Initiative provides a pathway for regulatory acceptance of dynamic tools for use in drug development programs. It represents a joint effort between OCP and OB.

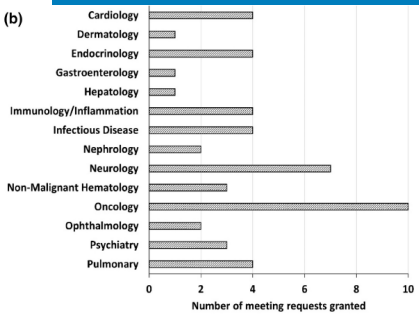
Disease	Tool	Trial
Alzheimer's Disease	Placebo/ disease progression	Trial Design
Multiple	MCP-Mod	Dose-finding
Multiple	Bayesian Optimal Interval (BOIN) design	Dose-finding
Multiple	Empirically Based Bayesian Emax Models	Dose-finding

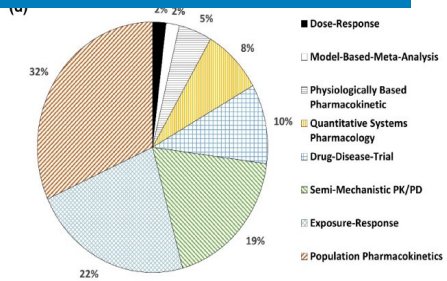
*: Drug Development Tools: Fit-for-Purpose Initiative | FDA

MIDD Meeting Program: Pilot to Pathway



MIDD Paired Meeting Pilot Program Summary





PERSPECTIVES

PERSPECTIVE

The US Food and Drug Administration's Model-Informed Drug Development Meeting Program: From Pilot to Pathway

Rajanikanth Madabushi[1,*], Jessica Benjamin[1], Hao Zhu[1] and Issam Zineh[1]

engagement on the application of MIDD approaches in drug development and review.

PILOT PROGRAM EXPERIENCE

High demand

The Pilot Program ran from 2018–2022 and committed to selecting 1 to 2 meeting requests per Center (Center for Drug Evaluation and Research and Center for Biologics Evaluation and Research) per quarter. Although the FDA and industry stakeholders involved in PDUFA VI negotiations mutually recognized the need for

Summary of the FDA Experience

IQ CLINICAL PHARMACOLOGY MIDD WORKING GROUP

CASE STUDY

INTERNATIONAL CONSORTIUM for INNOVATION & QUALITY in PHARMACEUTICAL DEVELOPMENT

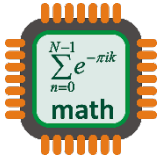
IQ shows FDA's MIDD Paired-Meeting Pilot Program has Demonstrable Benefits

THE CHALLENGE

Summary of Industry Experience

Policy Development

Global



Modeling

Clinical Pharmacology

Clinical

ICH M 15: MIDD Guidance

Pop-PK Guidance

Exposure-Response Guidance

PBPK Format and Content Guidance

Renal Impairment Guidance

Hepatic Impairment Guidance

Drug-Drug Interaction Guidance

Pediatrics Guidance

PD-1 & PD-L1 Alternative Dosing Guidance

Guidance for HIV-1 Treatment

Guidance for Pediatric Extrapolation Seizure treatment

Guidance for Ulcerative Colitis

Guidance for Hypertension

* This is an incomplete list of FDA and ICH guidances containing QM components.

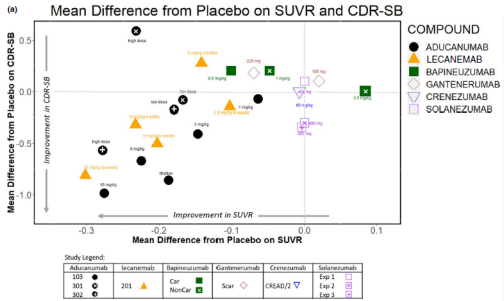
New Policy: Streamlined Drug Development

Drugs for Treatment of Partial Onset Seizures: Full Extrapolation of Efficacy from Adults to Pediatric Patients 2 Years of Age and Older
Guidance for Industry

It provides more efficient pathway for the development of effective treatment of partial onset seizure in pediatric patients 2 years and above

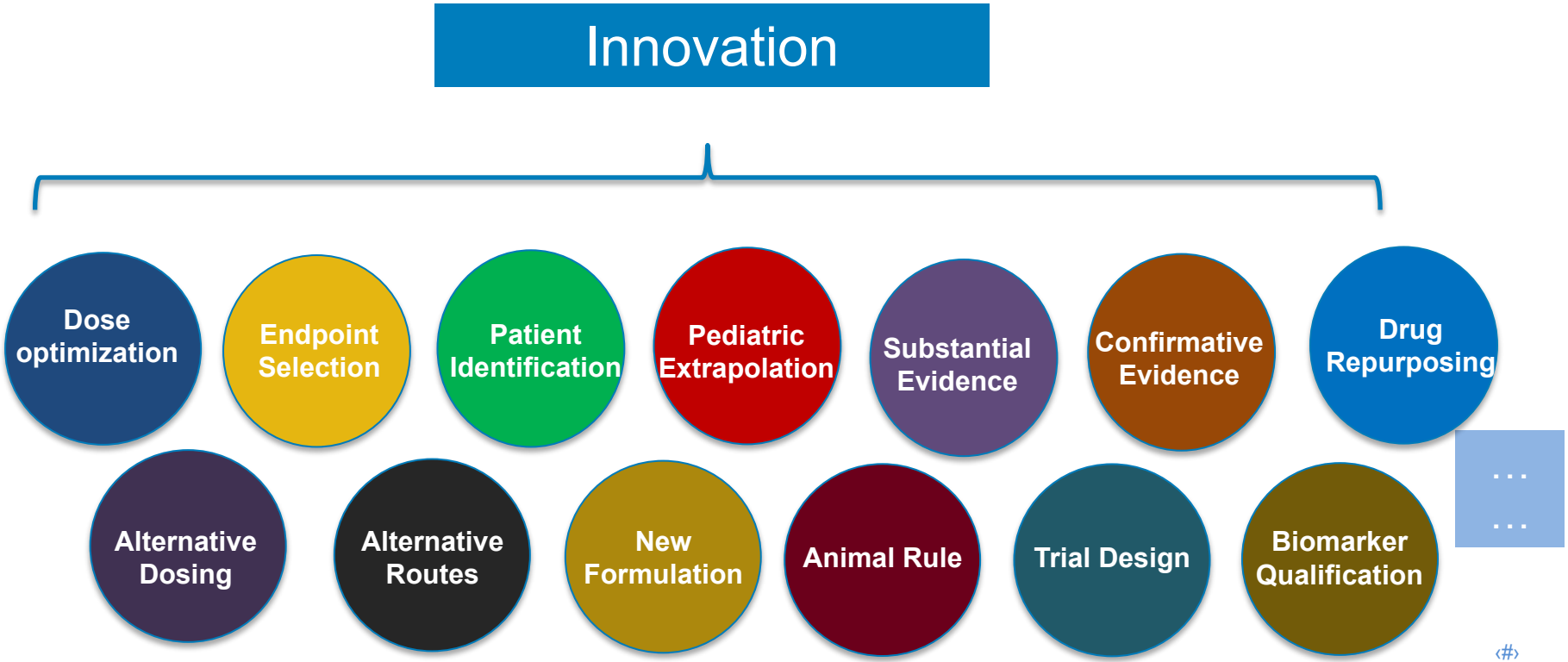
Pharmacokinetic-Based Criteria for Supporting Alternative Dosing Regimens of Programmed Cell Death Receptor-1 (PD-1) or Programmed Cell Death-Ligand 1 (PD-L1) Blocking Antibodies for Treatment of Patients with Cancer
Guidance for Industry

It allows efficient development of alternative dosing regimens for PD-1 and PD-L1 antibodies. It is especially valuable to protect vulnerable patients from contracting contagious diseases, such as COVID-19.



The evidence supports the use of reduction of beta-amyloid plaque as a reasonably likely surrogate endpoint to allow patient with Alzheimer's disease early access to a treatment intended to alter the underlying disease progression.

Current: Innovation for Drug Development



Quantitative Medicine Center of Excellence (For OCP)

Broader

Development

Streamlines new drug development so that an effective treatment may reach patients sooner

Deeper

Capability

Enhances our capability to promote the use of quantitative tools to streamline drug development

Synergized Effort

Provides opportunities for collaborations with internal and external stake holders.

Look forward to opportunities that the Quantitative Medicine Center of Excellence brings to all of us for the benefit of patients.

Acknowledgement

- Dr. Issam Zineh
- Dr. Raj Madabushi
- Dr. Shiew-Mei Huang
- Dr. Qi Liu
- FDA QM CoE Board Members
- OCP colleagues
- FDA QM CoE colleagues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Quantitative Medicine Innovations in the Generic Drug Program

Robert Lionberger
Director, Office of Research and Standards
Office of Generic Drugs
April 25, 2024

FDA Virtual Workshop entitled Streamlining Drug Development and Improving Public Health through Quantitative Medicine: An Introduction to the CDER Quantitative Medicine Center of Excellence

History of Modeling & Simulation in the Generic Drug Program

- Modeling and simulation critical to advances in bioequivalence (BE) science for systemically acting drugs (2003-2013)
  - Partial AUC, narrow therapeutic index drugs, highly variable drugs
- In 2014, OGD includes a Division of Quantitative Methods and Modeling (DQMM) in its reorganization

Core DQMM Teams

- Locally Acting Physiologically Based Pharmacokinetic (PBPK) Team
  - Mechanistic models for Topical, Inhalation, Nasal, Ophthalmic, Implantable routes
- Quantitative Clinical Pharmacology Team
  - Pharmacometrics models for bioequivalence studies
  - PK/PD and exposure response analysis for generic drug applications
- Oral Absorption Modeling Team
  - Models of the GI tract and drug absorption for systemic and locally acting drugs
- Data Science and Machine Learning Team
  - Machine learning and large language models focused on making the generic drug program more efficient by leveraging large data sets

Innovation driven by QM

- Local PBPK
  - FDA grant programs have supported the development and availability of PBPK models for local routes of actions
  - Critical to access to generic versions of inhalation, topical, ophthalmic and nasal products
  - Many generics of complex products are now approved without in vivo BE studies
- CFD (Computational Fluid Dynamics)
  - Mechanistic models for lung deposition and airflow in inhalation delivery devices
  - Physics based models used extensively in CDRH device evaluation
  - Innovative use in drug product development and review

Innovation driven by QM

- Machine Learning
  - Prediction of future ANDA submissions
  - Natural language tools for drug labels
  - More efficient model development (ML based QCP model selection)
- ICH M13 revisions
  - Models for food effect and fed bioequivalence
  - Supported significantly more efficient, globally harmonized BE study recommendations

Regulatory Impact Stories

- ANDA for topical gel approved without a clinical study because of a PBPK model for dermal absorption
- Model of drug delivery to the site of action was critical to support the acceptability of the applicants alternative BE approach

Tsakalozou, E., Babiskin, A. and Zhao, L. (2021), Physiologically-based pharmacokinetic modeling to support bioequivalence and approval of generic products: A case for diclofenac sodium topical gel, 1%. CPT Pharmacometrics Syst. Pharmacol., 10: 399-411. https://doi.org/10.1002/psp4.12600

- In FY23 20 topical ANDAs approved via in vitro only approaches
- In FY23, 2 topical ANDAs approved based on clinical endpoint BE

Innovation

- These innovations were developed to aid access to generic version of pharmaceutical products
- However, they are more broadly useful
- Through the CoE, more access across CDER programs to these type of innovations

In the Pipeline

- Model Informed Evidence (MIE) Meeting Pilot
  - For novel bioequivalence approaches that are more efficient because they combine a pre-specified model with data from in vivo or in vitro studies

- MIE Industry Meeting Pilot – General Principles, Sept. 12, 2023
  - https://www.fda.gov/media/172028/download?attachment

MIE for Long-Acting Injectables

- Consider a drug with three-month dosing interval for continuous use
  - Not safe for healthy subjects
  - Patients can't be washed out between T and R
  - Old thinking: Steady State BE
- MIE thinking
  - Switch before steady state with model-based correction for previous exposure

In the Pipeline

- Model Master File
  - Reusable
    - Efficient product development and application assessment
  - Scalable
    - More model submission in the future
  - Support an “Eco-system” for model development
    - Models are not just for applicants with “in-house” expertise
- May 2-3, 2024: Workshop: Considerations and Potential Regulatory Applications for a Model Master File
  - Register at https://www.complexgenerics.org/education-training/considerations-and-potential-regulatory-applications-for-a-model-master-file/

Summary

- The experience of the generic drug program is that Quantitative Medicine (modeling and simulation) supports innovation and access to equivalent product without unneeded clinical studies


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THE ROLE OF THE OFFICE OF BIOSTATISTICS

Stella Grosser
DBVIII/OB/OTS
April 25, 2024

Office of Biostatistics – Mission and Vision

- …Protect the public health by applying statistical approaches …for monitoring the effectiveness and safety of marketed drugs and therapeutic biologic products

- …We play a central role in promoting innovative, science-based, quantitative decision-making… throughout the drug-development life-cycle

QM-related PDUFA initiatives

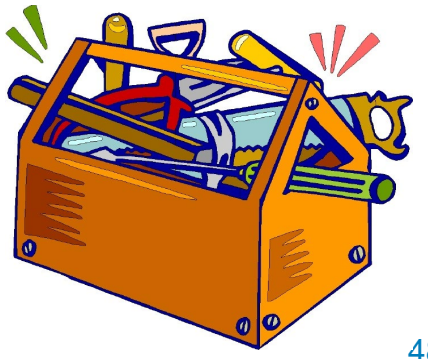
Office of Biostatistics plays important role in

- Model Informed Drug Development (MIDD)
- Fit for Purpose (FFP) reviews

MIDD as a Regulatory Tool

- Concept: Application of exposure-based, biological and statistical models to facilitate drug development and decision making.

- Regulatory tool: To promote early interaction between the drug developers and FDA on key issues.



MIDD: Leverage the Strengths of 2 Disciplines

While both disciplines may work on all aspects, they have particular strengths

Clinical Pharmacology:

- Understanding of principles of clinical pharmacology (PK & PD), patient characteristics, and diseases.
- Leading to adoption of useful predictions including extrapolation

Statistics:

- Separating exploration vs. confirmatory
- Detecting signal vs. noise, sometimes through advanced statistical tools
- Distinguishing association vs. causation, and promoting appropriate interpretation

Fit-for-Purpose (FFP) Initiative

- Provides a pathway for regulatory acceptance of dynamic tools for use in drug development programs.

- A drug development ool is deemed FFP based on the acceptance of the proposed tool following a thorough evaluation of the information provided

- The FFP determination is made publicly available in an effort to facilitate greater utilization of these tools in drug development programs

FFP – Types of Submissions

- **Leverage Strengths across Disciplines**
- **Statistical Models**
  - **model used to analyze and interpret data from experiments or clinical trials.**
  - **quantify relationships between variables, assess the significance of observed effects, and make predictions based on the data**
- Disease Models
  - simulate the progression of a disease over time.
  - capture the underlying biological and physiological treatments

FFP Determinations

Disease Area	Submitter	Tool	Trial Component	Issuance Date
Alzheimer's disease	The Coalition Against Major Diseases (CAMD)	Disease Model: Placebo/Disease Progression	Demographics, Drop-out	June 12, 2013
Multiple	Janssen Pharmaceuticals and Novartis Pharmaceuticals	Statistical Method: MCP-Mod	Dose-Finding	May 26, 2016
Multiple	Ying Yuan, PhD The University of Texas, MD Anderson Cancer Center	Statistical Method: Bayesian Optimal Interval (BOIN) Design	Dose-Finding	December 10, 2021
Multiple	Pfizer	Statistical Method: Empirically Based Bayesian Emax Models	Dose-Finding	August 5, 2022

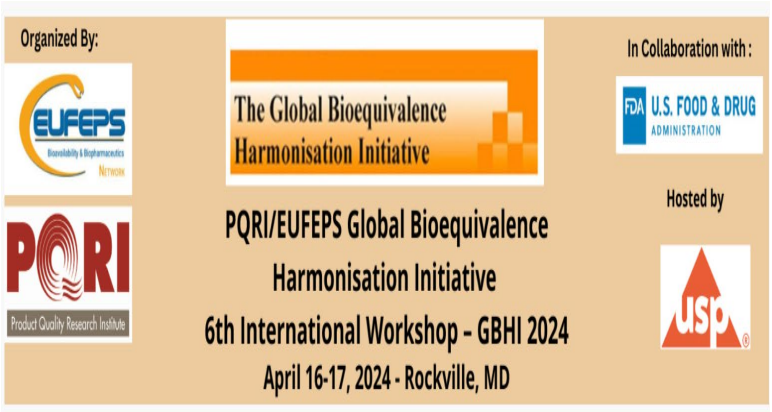
https://www.fda.gov/drugs/development-approval-process-drugs/drug-development-tools-fit-purpose-initiative

Empirically Based Bayesian Emax Models

Purpose	Impact
• Statistical methodology for dose finding clinical trials • Bayesian Emax model characterizes a relationship between drug efficacy and dosage level • To allow regulatory agents and users to more readily assess the safety of a trial	• Method works well for many of the prespecified compounds listed in the database; the prior specification for the Emax model appears acceptable for dose-response predictions • Tool and goodness-of-fit (GOF) statistic deemed Fit-For-Purpose with conditions • Agency recommends future Sponsors who intend to use the proposed tool should explore the performance of the proposed method in multiple studies and to meet with the Agency to discuss the prior information used for this tool

Other QM collaborations

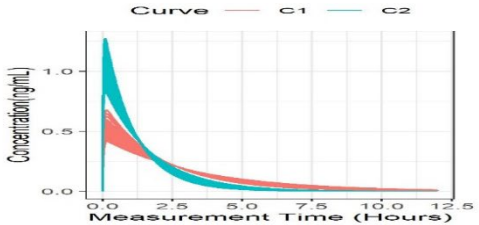
- Guidance and policy:
  - Narrow therapeutic index drugs
  - Product-specific guidances

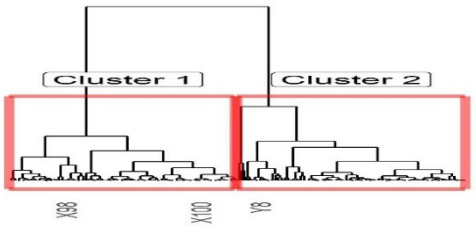


Other QM collaborations

Regulatory science research – internal and external

- **Application of Modeling and Simulation to Identify a Shortened Study Duration and Novel Bioequivalence Metric for a Long-Acting Intrauterine System** *AAPS J* 2022 May 2;24(3):63. doi: 10.1208/s12248-022-00715-z.
- **Model-based bioequivalence approach for sparse pharmacokinetic bioequivalence studies: model selection or model averaging?** Accepted to *Statistics in Medicine*
- **Applications of Machine Learning in Pharmacogenomics: Clustering Pharmacokinetic Concentration Curves.** Submitted, under revision





Current and Future Opportunities

- Rare Diseases
  - Small samples
  - incorporate quantitative aspects of known biology and natural history,
  - innovative trial designs
- AI/ML in review of regulatory submissions, drug safety

Future Opportunities

Future Opportunities

Bring together different perspectives and expertise

Make progress on difficult questions and meet emerging regulatory and public health needs

Panel Discussion

Charting the Course:

CDER Perspectives on Quantitative Medicine Opportunities

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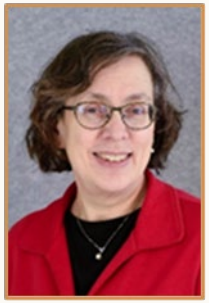
Moderator:

Issam Zineh, PharmD, MPH, FCP, FCCP
FDA OCP



Stella Grosser, PhD
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FDA Workshop

Streamlining Drug Development and Improving Public Health through Quantitative Medicine

Break

CDERQuantMed@fda.hhs.gov

Panel Discussion

Needs, Gaps, and Opportunities in Quantitative Medicine:

A Multistakeholder Discussion on Education/Outreach, Policy Development, Stakeholder Engagement

Needs, Gaps, and Opportunities in Quantitative Medicine

Moderator:

Rajanikanth Madabushi, PhD
FDA OCP

Joga Gobburu, PhD, MBA

University of Maryland, Baltimore

Dan Hartman, MD

Bill and Melinda Gates Foundation

Lisa LaVange, PhD

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Cynthia J. (C.J.) Musante, PhD

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Stacey Tannenbaum, PhD, FISoP

Metrum Research Group

Embracing Interdisciplinary Innovation and Promoting Regulatory Science Excellence in Quantitative Medicine: Summary of Key Points

Larry Lesko, PhD, FCP,
University of Florida College of Pharmacy

Embracing Interdisciplinary Innovation and Promoting Regulatory Science Excellence in Quantitative Medicine: Summary of Key Points

Lawrence J. Lesko, Ph.D., F.C.P.

Clinical Professor Emeritus and Founding Director of the University of Florida Center for Pharmacometrics and Systems Pharmacology

April 25, 2024

Innovation or Stagnation?

When Dr. Janet Woodcock, then Director of CDER, introduced her page-turning, white paper on the *FDA's Critical Path Initiative* in March 2004, about the significance of regulatory science, she personally transformed the culture of FDA to embrace the concept of *model-based drug development.*

The CPI Opportunities List in 2006 was a targeted effort to advocate building pharmaco-statistical models to analyze drug efficacy and safety information, and to *improve drug development and regulatory decision-making*.

One of the Most Enduring Opportunities of the CPI Has Been the Concept of Model-Based Drug Development

Its principles live on and have been embedded in almost every new FDA regulatory science program in the past 20 years.

"*Modeling and simulation* can also inform regulatory decisions, making the product development process more efficient and reducing uncertainty. Almost 100% of all new drug applications for new molecular entities have components of *modeling and simulation*."

Dr. Scott Gottlieb, FDA Commissioner, September 2017 speech to RAPS

From a scientific perspective, the predictions of Drs. Woodcock and Gottlieb have become reality. Technology is constantly evolving, and the QM CoE represents a way for CDER to adapt for future regulatory science to thrive.

"The goal of the newly established CDER QM CoE is intended to spur innovation and foster comprehensive and consistent integration of *quantitative modeling and simulation* approaches across CDER and to facilitate interdisciplinary collaboration."

FDA Announcement, March 25, 2024

How Will the QM CoE Shape the Trajectory of Regulatory Science?

Past | **WE ARE HERE** | **Future**

Composite success of MBDD → Fulfillment of CoE success criteria

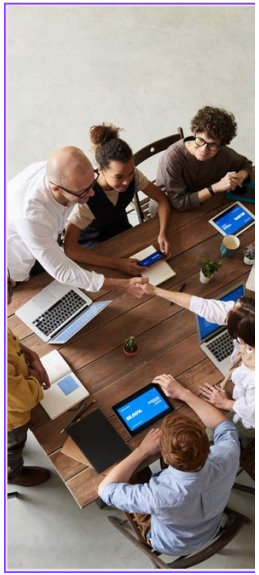
- Many use cases across a panorama of M&S platforms
- Regulatory guidances that lay out best practices
- MIDD paired FDA-industry meetings focused on implementation
- Regulatory science research on new methodologies

Policy development
Best practices
Stakeholder outreach
Education and training

Beacon of progress for QM enhanced with modern quantitative tools to navigate the decision-making framework of MIDD

Adopt the Long View: Changes in CDER Organization Take Time and Perseverance, and Occur Gradually

A breakdown of 3 success factors: it's easier said than done.



1) Critical to success is *people and culture*. Getting each office on board can be a challenge -- different disciplines juggle different priorities. A shared data-driven and model mind-set will help get things off the ground.

2) Creating demand facilities *adoption*. Seed the pipeline of the CoE work with curated examples with high value and good chance of collaborative success – in other words, "quick wins" or "low-hanging fruit".

3) Identify *evangelists.* People that enthusiastically support and promote the CoE to a wide audience internally and externally. Raise awareness, identify partnering opportunities with stakeholders and listen seriously to feedback to iterate strategy on what is learned.

A Page Out of the QM CoE Playbook: Building the Plane While Flying It

Key Takeaway: The More Boxes the QM CoE Can Check, the Greater the Likelihood of Success

- ✓ Leadership endorsement and buy-in
- ✓ Well-defined and aspirational vision
- ✓ Four specific goals to achieve the vision
- ✓ Clear expectation of participation by each office
- ✓ Commitment to collaborate across disciplines
- ✓ Shared tangible and persuasive benefits

To sum it up: the QM CoE is poised to become an innovation hub fostering pinnacle performance in quantitative medicine

Congratulations! What a great start today.

We all will be following the work of the CoE as a compass for navigating the landscape of essential quantitative methods and progress in transforming quantitative medicine.

Next Steps & Outlook for the Future

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FDA OCP

Thank you for joining!

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