FDA/CDER Virtual Workshop

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

Program Book

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Workshop Overview

Date: April 25, 2024

Time: 9:00 am-1:00 pm (ET)

Location: Zoom

About This Event:

This virtual workshop will be hosted by the newly established FDA Center for Drug Evaluation and Research (CDER) Quantitative Medicine Center of Excellence (QM CoE). The purpose of this workshop is to introduce the CDER QM CoE, providing an overview of the scope, goals, and current state, while gaining feedback from the public on needs and opportunities in education, outreach, and policy.

Background:

QM involves 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. The newly established CDER QM CoE is a coordinating body intended to spur innovation and foster comprehensive integration of QM approaches to advance therapeutic medical product development and promote public health. As part of its goal to engage the drug development, research, and patient communities, the QM CoE is holding this workshop to orient stakeholders its mission and scope and to dialogue on opportunity areas.

Workshop Objectives:

- Provide an overview of the newly formed QM CoE, including discussion of the current goals, initiatives, and priority areas
- Engage with stakeholders to inform future QM CoE initiatives in education, outreach, and policy development

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For questions regarding this event, please contact CDERQuantMed@fda.hhs.gov.

Agenda

Time (ET)	Presentation	Speaker(s)
9:00 am - 9:10 am	Opening Remarks	Patrizia Cavazzoni, MD, CDER Director/FDA
9:10 am - 9:25 am	Introduction to the CDER Quantitative Medicine Center of Excellence	Raj Madabushi, PhD, OCP/QM CoE Director/FDA
9:25 am - 9:40 am	Quantitative Medicine in the Office of Clinical Pharmacology: From the Past to the Future	Hao Zhu, PhD, OCP/FDA
9:40 am - 9:55 am	Quantitative Medicine Innovations in the Generic Drug Program	Robert Lionberger, PhD, OGD/FDA
9:55 am - 10:10 am	The Role of Biostatistics in Quantitative Medicine – From Evidence to Inference and Beyond	Stella Grosser, PhD, OB/FDA
10:10 am - 11:10 am	Charting the Course: CDER Perspectives on Quantitative Medicine Opportunities	**Moderator:** Issam Zineh, PharmD, MPH, FCP, FCCP, OCP/FDA **Panelists:** Stella Grosser, PhD, OB/FDA Qi Liu, PhD, OCP/FDA Nikolay Nikolov, MD, OND/FDA Bhagwant Rege, PhD, OPQ/FDA James Smith, MD, MS, OND/FDA Liang Zhao, PhD, OGD/FDA
11:10 am - 11:30 am	Break	
11:30 am - 12:40 pm	Needs, Gaps, and Opportunities in Quantitative Medicine: A Multistakeholder Discussion on Education/Outreach, Policy Development, Stakeholder Engagement	**Moderator:** Raj Madabushi, PhD, OCP/QM CoE Director/FDA **Panelists:** Joga Gobburu, PhD, MBA, University of Maryland School of Pharmacy Dan Hartman, MD, Bill and Melinda Gates Foundation Lisa LaVange, PhD, University of North Carolina at Chapel Hill CJ Musante, PhD, Pfizer Stacey Tannenbaum, PhD, FISoP, Metrum Research Group
12:40 pm - 12:50 pm	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
12:50 pm - 1:00 pm	Next Steps & Outlook for the Future	Issam Zineh, PharmD, MPH, FCP, FCCP, OCP/FDA

Speaker & Panelist Biographies

Opening Remarks

Patrizia Cavazzoni, MD, is the Director of the Center for Drug Evaluation and Research (CDER) at the U.S. Food and Drug Administration (FDA). The Center's mission is to ensure that safe, effective and high-quality drugs are available to the public. To achieve this goal, CDER regulates the medical products under its jurisdiction throughout their lifecycle, oversees the development of new and generic drugs, evaluates applications to determine whether drugs should be approved, monitors the safety of drugs after they are marketed, conducts research to advance regulatory science, and takes enforcement actions to protect the public from harmful products. Dr. Cavazzoni joined the FDA in January 2018 as CDER's Deputy Director for Operations where she led several key initiatives on behalf of the organization. She also served as Acting Principal Deputy Commissioner of Food and Drugs from January 2019 to February 2019. Dr. Cavazzoni received her medical degree at McGill University and completed a residency in psychiatry and a fellowship in mood disorders at the University of Ottawa. During her training, she was an investigator in clinical trials of novel antipsychotic and antidepressant medications and became a research collaborator within the International Group for The Study of Lithium Treated Patients. She subsequently received a full-time appointment to the Faculty of Medicine at the University of Ottawa and joined the Mood Disorders Program at the Royal Ottawa Hospital, where she treated patients suffering from severe mood disorders, taught students, and conducted research on genetic predictors of bipolar disorder as part of a multidisciplinary international collaborative effort, authoring numerous peer-reviewed scientific publications. After her tenure in academic medicine, Dr. Cavazzoni worked in the pharmaceutical industry for several years and held senior executive positions in clinical development, regulatory affairs, and safety risk management in large companies across multiple therapeutic areas, until she joined the FDA. Dr. Cavazzoni obtained certification by the American Board of Neurology and Psychiatry in 1997 and 2008 and was a fellow of the Canadian Royal College of Physicians and Surgeons from 1997 until 2023. She is a fellow of the Canadian College of Neuropsychopharmacology and a recipient of the American College of Psychiatrists' Laughlin Fellowship.

Introduction to the CDER Quantitative Medicine Center of Excellence

Rajanikanth (Raj) Madabushi, PhD, has over 15 years of regulatory experience as a Pharmacometrics Reviewer and Clinical Pharmacology Team Lead in the Office of Clinical Pharmacology (OCP), Office of Translational Sciences (OTS) at CDER/FDA. He currently serves as the Associate Director, Guidance and Scientific Policy in OCP and the Director of the CDER Quantitative Medicine Center of Excellence. Dr. Madabushi plays an instrumental role in FDA's PDUFA MIDD initiatives and is the CDER Point-of-Contact for the MIDD Paired Meeting Program. Dr. Madabushi is also involved in global harmonization activities as the Rapporteur for ICH M12 Expert Working Group – Drug Interaction Studies. Dr. Madabushi received his PhD in Pharmaceutical Sciences from Birla Institute of Technology and Sciences (BITS), Pilani, India.

Quantitative Medicine in the Office of Clinical Pharmacology: From the Past to the Future

Hao Zhu, PhD, is the Director of the Division of Pharmacometrics, OCP/OTS/CDER/FDA. Dr. Zhu received his PhD in Pharmaceutical Sciences and Masters in Statistics from the University of Florida. He started his career in modeling and simulation teams at Johnson & Johnson and Bristol-Myers-Squibb. He joined FDA as a pharmacometrics reviewer more than 17 years ago. Dr. Zhu has been a clinical pharmacology team leader for more than 6 years and a QT-IRT scientific lead for 2 years. Then he became the Deputy Director for the Division of Pharmacometrics. His Division reviews pharmacometrics-related submissions and supports pharmacometrics-related policy development.

Quantitative Medicine Innovations in the Generic Drug Program

Robert Lionberger, PhD, serves as Director of the Office of Research and Standards (ORS) in the Office of Generic Drugs (OGD) at CDER/FDA. Dr. Lionberger leads OGD's implementation of the GDUFA science and research commitments including internal research activities and external research grants and collaborations to ensure the therapeutic equivalence of generic drug products. ORS also provides pre-submission advice on complex generics through pre-ANDA meetings, product specific guidance and correspondence responses. He received his undergraduate degree from Stanford University in Chemical Engineering, and a PhD from Princeton University in Chemical Engineering. After his PhD, he conducted post-doctoral research in Australia in the Department of Mathematics and Statistics at the University of Melbourne. Prior to joining the FDA 20 years ago, he was an Assistant Professor of Chemical Engineering at the University of Michigan.

The Role of Biostatistics in Quantitative Medicine – From Evidence to Inference and Beyond

Stella C. Grosser, PhD, is the Director of Division of Biometrics 8 in the Office of Biostatistics (OB), OTS/CDER/FDA. She has decades of experience in biomedical research and consulting. Dr. Grosser has been at the FDA for over 20 years, beginning as a statistical reviewer for new drug products and serving as a team leader before assuming her current position. She received her PhD in biostatistics from UCLA and spent several years there afterwards as an assistant professor in the School of Public Health. She holds a BA in mathematics from Yale University and an MS in mathematical statistics from Stanford.

Panel Discussion - Charting the Course: CDER Perspectives on Quantitative Medicine Opportunities

Issam Zineh, PharmD, MPH, FCP, FCCP, is Director of the Office of Clinical Pharmacology (OCP) at the FDA. He has held various leadership positions at FDA including Associate Director for Genomics in OCP (2008-2012) and Co-Director of the CDER Biomarker Qualification Program (2009-2015) and serves on the CDER Medical Policy Council. He is a recognized expert in the fields of drug development and evaluation, clinical pharmacology, pharmacotherapy, and precision medicine. As Director of OCP, Dr. Zineh leads a staff of over 280 regulatory, research, program/project management, and administrative staff in FDA's efforts to enhance drug development and promote regulatory innovation through clinical pharmacology and experimental medicine.

Qi Liu, PhD, MStat, FCP, is the Associate Director for Innovation & Partnership in OCP, OTS/CDER/FDA. She leads OCP's innovative initiatives through strategic partnership. She has helped develop OCP's portfolio on machine learning/artificial intelligence, real-world evidence, and digital health technologies, collaborating with internal and external experts. She led OCP's Physiologically Based Pharmacokinetic Modeling and Simulation Oversight Board and co-led the Biologics Oversight Board. She was also a co-lead initiating the Real-Time Oncology Review and Assessment Aid Pilot Programs. During her career at the FDA, she also contributed to over 200 NDA/sNDA reviews, 20 BLA/sBLA reviews, and numerous IND reviews to support drug development. She worked on working groups for FDA guidance documents and Manual of Policies & Procedures. She is an Associate Editor of Clinical Translational Science and on the editorial board of five scientific journals. Before joining FDA, Dr. Liu was a senior pharmacokineticist at Merck & Co. Inc. She obtained her PhD degree in Pharmaceutics and a concurrent Master's degree in Statistics from the University of Florida in 2004. In addition, she has a Master's degree in Pharmaceutics and a Bachelors' degree in Clinical Pharmacy from West China University of Medical Sciences.

Nikolay P. Nikolov, MD, is a board-certified Internist and Rheumatologist who joined FDA in 2009 as a Medical Officer and is currently the Director of the Office of Immunology and Inflammation in OND/CDER. He completed his Internal Medicine residency at Lincoln Medical Center, Bronx, NY in 2002 and then joined the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), NIH, where he completed his rheumatology fellowship in 2004, participated in clinical investigational protocols and studied cellular and molecular mechanisms of autoimmunity in animal models in the Immunoregulatory Group, Autoimmunity Branch at NIAMS. In 2005, Dr. Nikolov joined the Sjögren's Syndrome Group at the National Institute of Dental and Craniofacial Research, NIH, as a clinical investigator where he conducted clinical and translational protocols in systemic lupus erythematosus (SLE) and Sjögren's syndrome. At the FDA, Dr. Nikolov is involved in the regulatory review of immuno-modulatory therapies, including small molecules, biologics and biosimilars, for the treatment of pediatric and adult diseases. He has also participated in the development of the Agency's policies in these areas.

James P. Smith, MD, is the Director of the Office of New Drug Policy, OND, previously having held various leadership positions within the office since its formation in 2018. Prior to his roles in OND Policy, he held positions as a primary reviewer, team leader, and Deputy Division Director of the former Division of Metabolism and Endocrinology Products after joining the FDA in 2011. Dr. Smith has overseen development programs targeting diseases ranging from the very rare to the very common, and his specific interests include clinical, scientific, and policy considerations related to generating evidence to demonstrate the safety and effectiveness of new drugs and biological products. Dr. Smith is a graduate of the University of Michigan Medical School and completed an Internal Medicine residency at the same institution before fellowships in both nephrology and clinical pharmacology at Vanderbilt University Medical Center. He also holds a master's degree in Clinical Research Design and Statistical Analysis from the University of Michigan School of Public Health.

Bhagwant Rege, PhD, is the Division Director for Biopharmaceutics in OPQA I/OPQ/CDER at the FDA. His division at FDA is responsible for assessment of clinically relevant in vitro release specifications for drug products, in vitro-in vivo correlations (IVIVC), physiologically based biopharmaceutics models (PBBM), scientific bridging strategies, biowaivers, and BCS classification requests. Most recently he served as Division Director for CDER/OPQ/OLDP/ Division of Immediate and Modified Release Products III. Prior to joining FDA in 2010, he worked in industry for many years in oral biopharmaceutics and formulation development groups. Bhagwant has served as a team leader and review chemist in OGD where he was part of the team that developed the QbD examples for the generic industry. He is a member of the FDA Emerging Technology Team (ETT) and ICH Q12 Expert/Implementation Working Group. He served as FDA liaison on the USP expert committee on dosage forms general chapter (2015-2020). Bhagwant received his BS and MS in pharmacy from the University of Mumbai, India and a PhD in Pharmaceutical Sciences from the University of Maryland, Baltimore.

Liang Zhao, PhD, has been the Director of Division of Quantitative Methods and Modeling (DQMM), Office of Research and Standards, OGD/CDER/FDA since 2015. He has demonstrated excellence and leadership in drug development and regulatory science for new and generic drugs during his 19-year professional tenure including in Pharsight as an associate consultant, BMS as a research investigator, MedImmune as an Associate Director, and FDA as Clinical Pharmacology reviewer, Pharmacometrics Team Leader, and Division Director. Dr. Zhao and his team have introduced a broad array of innovative tools in the realm of drug delivery, bioequivalence assessment, and big-data tools including machine learning to pharmacometrics. They have also implemented the Model Integrated Evidence (MIE) Industry Meeting Pilot to support regulatory communications between generic applicants and the FDA and proposed a regulatory mechanism of using Model Master File to support regulatory submissions. Liang currently serves as the Chair of the FDA ModSim WG for the Modeling & Simulation community cross FDA centers and offices. He has published over 110 peer-reviewed publications and 8 book chapters. He received the 2023 Gary Neil Prize for Innovation in Drug Development from ASCPT in recognition to his contribution to clinical pharmacology and pharmacometrics.

Panel Discussion - Needs, Gaps, and Opportunities in Quantitative Medicine: A Multistakeholder Discussion on Education/Outreach, Policy Development, Stakeholder Engagement

Joga Gobburu, PhD, MBA, is a Professor at the University of Maryland, Baltimore, MD, USA. With a rich background at the US FDA spanning from 1998 to 2011, he brings extensive expertise in regulatory affairs and drug approval processes. During his tenure, he oversaw the review of numerous INDs, NDAs, and BLAs, contributing significantly to FDA guidances and policies on drug approval and labeling. His exceptional contributions were recognized with prestigious awards, including the FDA's Outstanding Achievement Award and the Senior Biomedical Research Scientist appointment. Additionally, he has been honored with awards from leading organizations such as the American Conference on Pharmacometrics and the American College of Clinical Pharmacology. Dr. Gobburu's scholarly impact is evident through his extensive publication record, comprising over 120 papers and book chapters, and his editorial roles in several esteemed journals.

Dan Hartman, MD, joined the Bill and Melinda Gates foundation in 2012 as the director of Integrated Development and leads a team that provides technical expertise in product development. Under his leadership, Integrated Development works closely with the foundation's disease strategy teams to manage product pipelines from late discovery through registration by providing state-of-the-art input in the areas of quantitative sciences/pharmacology, chemical manufacturing, and regulatory strategy. Integrated Development also manages investments in a variety of areas that will benefit numerous foundation strategies, most notably in the areas of regulatory systems, pharmacology focused model-based drug development, big data programs, novel formulations (including pediatrics) and low-cost manufacturing. From 2016-2018, he took on additional responsibility as the interim director of the Malaria program strategy, guiding the foundation's efforts towards eradication. He is currently a senior advisor to the Malaria team. Dan has extensive management and pharmaceutical development experience. He joined the foundation after four years as president and CEO of Great Lakes Development Inc., a consulting company providing strategic and operational support for early drug development projects. Previously, he served as senior vice president of Product Development at deCODE genetics, executive director of Pfizer Global Research and Development, vice president of Global Clinical Development at Esperion Therapeutics, and clinical research positions at Eli Lilly & Company. He has also provided consultation to the biopharmaceutical venture capital community and serves as a member/advisor to several non-profit boards. Dan served as a member of the NIH National Center for the Advancement of Translational Sciences (NCATS) and Cures Acceleration Network advisory board from 2016-2019. He was president of the American Society of Clinical Pharmacology and Therapeutics and the recipient of numerous awards including National Inventor of the Year in the Unites States. He received his bachelor's degree from Calvin College and his medical degree from Wayne State University. He trained in medicine and completed a fellowship in pulmonary medicine from Indiana University, where he was also chief medical resident.

Lisa LaVange, PhD, is Professor Emerita and former Chair of the Department of Biostatistics in the Gillings School of Global Public Health at the University of North Carolina at Chapel Hill. She is also former director of the department's Collaborative Studies Coordinating Center (CSCC), the longest-running NIH-funded coordinating center for large-scale clinical trials and epidemiological studies. From 2011 to 2017, Dr. LaVange was director of the Office of Biostatistics in FDA's CDER. There, she oversaw more than 200 statisticians and other staff members involved in the development and application of statistical methodology for drug regulation. She was a leader in developing and assessing the effectiveness and appropriateness of innovative statistical methods intended to accelerate the process from drug discovery to clinical trials to FDA approval and patients' benefit. Prior to her government and academic experience, she spent 16 years in non-profit research and 10 years in the pharmaceutical industry. Dr. LaVange is an elected fellow of the American Statistical Association (ASA) and was the 2018 ASA President. She was the 2007 President of the Eastern North American Region of the International Biometric Society (IBS - ENAR) and former member of the IBS Executive Board. In 2020, she received the Drug Information Association (DIA) Inspire Award for Outstanding Contribution to Health in the Americas Region. In 2023, she received the International Council on Harmonisation (ICH) Award for Outstanding Contribution to ICH Harmonisation for Better Health.

Cynthia J. (C.J.) Musante, PhD, is Vice President of Scientific Research and Global Head of Pharmacometrics & Systems Pharmacology (PSP) at Pfizer Inc. She received her PhD in Applied Mathematics from North Carolina State University and has more than twenty years of experience in model-informed drug development (MIDD). At Pfizer, her team is responsible for developing and applying model-based approaches across the portfolio to enhance the robustness and quality of decision-making at the program- and therapeutic strategy-level. CJ is an advocate for MIDD, both internally and externally. She is a frequent organizer and invited speaker at national and international conferences and is the Immediate Past President of the International Society of Pharmacometrics (ISoP).

Stacey Tannenbaum, PhD, FISoP, is the Vice President of Scientific Engagement at Metrum Research Group. Prior to joining MetrumRG, she had 20 years of Modeling and Simulation experience in Pharma, first at Novartis and then Astellas; during her last 5 years at Astellas she was the lead of the US Pharmacometrics group. Stacey completed her BSE in Biomedical Engineering at Duke University, and her PhD in Pharmaceutical Sciences and Applied Mathematics at the University of Arizona, followed by a post-doctoral fellowship at the Center for Drug Development Science at Georgetown University. She holds faculty positions at the University of Arizona, University of the Pacific, and the University of Tennessee Health Science Center. Stacey has had significant impact on the global Pharmacometrics community by co-founding the International Society of Pharmacometrics (ISoP), serving as its first President, and sits on a number of ISoP committees and interest groups, including leadership on the Statistics and Pharmacometrics Special Interest Group. She received the ISoP Fellowship in 2014 and Leadership Award in 2018. Stacey co-founded the American Conference on Pharmacometrics (ACoP) and was conference chair for the first three events. She was a co-founder of the local networking group Modeling and Simulation Applications in Clinical Pharmacotherapy (MoSAiC) and is the Executive Committee chair for the World Conference on Pharmacometrics (WCoP). She served

as a board member of the American Association of Pharmaceutical Scientists (AAPS), chaired the AAPS M&S Focus Group, and was the co-chair for the AAPS Forum for Connecting Predictive Modelers. She is also the chair elect of the Quantitative Pharmacology Network at the American Society of Clinical Pharmacology and Therapeutics (ASCPT).

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

Lawrence Lesko, PhD, FCP, is Clinical Professor Emeritus at the University of Florida College of Pharmacy in Lake Nona, Florida. He was the Founding Director of the UF Center for Pharmacometrics and Systems Pharmacology in 2011. Dr. Lesko was formerly the Director of the Office of Clinical Pharmacology in CDER/FDA from 1995 to 2011. He established regulatory programs in pharmacometrics, mechanistic QSP models of adverse drug events, and pharmacogenomics. Dr. Lesko has received many awards including ASCPT's Rawls-Palmer Progress in Medicine Award, Gary Neil Prize for Innovation in Drug Development Award, and the FDA-William Abrams Lecture Award. He also received the International Society of Pharmacometrics Leadership Award. He is a Fellow in the Japanese Society of Xenobiotics, the College of Physicians of Philadelphia, the American College of Clinical Pharmacology and AAPS. Dr. Lesko has authored over 225 peer-reviewed articles and is Board Certified in Applied Pharmacology. He currently serves as a drug development and regulatory consultant to the pharmaceutical industry.