U.S. FOOD & DRUG ADMINISTRATION

2023 FDA Science Forum

Advancing Regulatory Science Through Innovation

June 13-14, 2023

2023 FDA Science Forum

Advancing Regulatory Science through Innovation

Tuesday, June 13, 2023 and
Wednesday, June 14, 2023

Virtual Webcast

2023 FDA Science Forum

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A Message from the FDA Commissioner

Robert M. Califf, PhD
Commissioner, FDA

Nearly every day of the year, the FDA is host to a variety of important public meetings, conferences symposia, and other significant events to help inform scientists and the public, to advance innovation in the scientific enterprise, and to support our mission to protect and promote public health. The FDA Science Forum is an especially important event on the FDA calendar because rather than focusing on one particular area of science, it is designed to highlight the enormous expanse of scientific expertise and inquiry for which the FDA is responsible. This meeting is particularly exciting under the leadership of Dr. Bumpass — I've learned a lot from her already, and her impact on science at the FDA will be profound.

A quick look at the breadth of topics to be covered in this year's gathering confirms this. The sessions are as wide-ranging as substance abuse, big data, medical countermeasures, infectious disease, and pathogen reduction technologies, and patient empowerment, to name just a few of the topics. The breadth of the issues and challenges we face, as well as the expanse of expertise we have to respond to them, is abundantly clear.

We must stay ahead of the scientific curve by embracing and developing cutting edge science and technology that supports new and powerful innovations in regulatory science. It is equally essential that we strengthen the means for acquiring, reviewing, and evaluating data, in order to ensure that we have the newest and best evidence to inform our scientific work and the decisions we make.

Science, by its nature, involves a constantly changing body of information, data, and evidence. Indeed, this quality of scientific inquiry is not only one of the most challenging and exciting aspects of science, but also among the most gratifying.

The FDA workforce is uniquely prepared and equipped to respond to these challenges. We have an enormous wealth of expertise across many different scientific, medical, and regulatory disciplines that include a diversity of perspectives and approaches. We also engage in partnerships and collaborative efforts with industry, academia, patient advocacy organizations, government, and other stakeholders.

While the importance of science and the scientific mission is central to our work and the Office of the Chief Scientist, which hosts this gathering, this mission is increasingly complicated by a growing dissemination of misinformation and disinformation about science. Even as all of you have committed yourselves to the application of science and scientific integrity, there are many who are working to destabilize your important efforts.

I've spoken often about this development, both because it is causing enormous harm to the health of Americans, as people are misled into making bad, dangerous, and uninformed choices, and also because it has the potential

to undermine the important scientific work that the FDA, other government agencies, industry, academia, and other groups are engaged in to help protect public health and advance innovation.

While this topic is not specifically on the agenda of this meeting, I hope you will include discussion of it as part of the other topics you will be addressing. In addition to doing science, the ability to explain science to non-scientists is a skill that we all need to acquire and hone. We also need to have the courage to directly address misinformation when we encounter it.

A meeting such as this offers an excellent opportunity for sharing information and developing new strategies to advance the important work you are doing. It will require all of us working together to improve the level of trust in science and medicine.

Thank you for participating in this year's Science Forum, and I hope you have a successful and productive meeting.

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A Message from the FDA Chief Scientist

Namandjé N. Bumpus, PhD
Chief Scientist, FDA

It is my pleasure to welcome you to the 2023 FDA Science Forum. There are over 11,000 scientists working at the FDA, and the Science Forum gives you an opportunity to hear about some of their work.

First, you will hear from our keynote speaker, Dr. Murray Lumpkin, Deputy Director of Integrated Development, Bill & Melinda Gates Foundation. Dr. Lumpkin previously spent 24 years at the FDA. During his time here, he served as Director of the Division of Anti-Infective Drug Products; Deputy Center Director, Review Management, Center for Drug Evaluation and Research; Deputy Commissioner for International and Special Programs; and the FDA Commissioner's Senior Advisor and representative for global issues. He was a dynamic leader at the FDA and continues to be an innovator in the field of regulatory science, so we are excited to have him with us again to kick off this important event.

The subsequent presentations will cover eight key objectives that highlight scientific research across the scope of the FDA mission. The FDA is charged with ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices; and ensuring the safety of our nation's food supply, cosmetics, and products that emit radiation, to ultimately protect the health of the American people. The research conducted here, and in partnership with academic research centers, contributes to this mission and forms the foundation for our regulatory decision-making.

To note a few examples — you will hear from the Center for Biologics Evaluation and Research and the Center for Drug Evaluation and Research about their work to advance real-world evidence. Scientists from the Center for Food Safety and Applied Nutrition will speak about their work on new alternative methods. Researchers from the Center for Tobacco Products will present on tobacco regulatory research in different populations. You will hear about educational projects from the Center for Veterinary Medicine's Veterinary Laboratory Investigation and Response Network. Scientists from the Center for Devices and Radiological Health will speak about the use of medical devices in public health emergencies. Scientists from the National Center for Toxicological Research and the Office of Cosmetics and Colors will give an update on their collaborative efforts to support cosmetics safety evaluation. Scientists from the Office of Regulatory Affairs will present on their analytical toolkit to identify potentially harmful active pharmaceutical ingredients in mail entering the United States.

It is my hope that by attending this year's FDA Science Forum, you obtain a greater understanding of the scope of the work done at the FDA. As chief scientist I strive to make our science more accessible, inviting the public to learn about and engage with the science we do every day. We take pride in our efforts to share and collaborate with the public and with our colleagues in academia, industry, and sister

agencies. I hope you enjoy what we share with you today, and I look forward to future opportunities to share with you again. Thank you for joining us.

Keynote Speaker

Murray Lumpkin, MD

Deputy Director, Integrated Development, Regulatory Affairs

Bill & Melinda Gates Foundation

Dr. Murray Lumpkin leads global regulatory systems initiatives for the Bill & Melinda Gates Foundation. In this role, he works with partners (including the World Health Organization, regionalization initiatives, and national regulatory authorities) to optimize the regulatory processes through which products must pass to be developed, legally marketed, and procured in low- and middle-income countries, without sacrificing product quality, efficacy, or safety.

Before joining the foundation in 2014, Murray had a 24-year career at the Food and Drug Administration. His roles included Director of the Division of Anti-Infective Drug Products; Deputy Center Director, Review Management, the Center for Drug Evaluation and Research; Deputy Commissioner for International and Special Programs; and the FDA Commissioner's Senior Advisor and Representative for Global Issues.

Murray is a medical doctor and a fellow of the American Academy of Pediatrics. He had fellowships in pediatrics and pediatric infectious diseases at the Mayo Clinic and was a Fulbright scholar in the United Kingdom, where he received an MS in Medical Parasitology and a diploma in tropical medicine and hygiene from the London School of Hygiene and Tropical Medicine. He worked at a refugee clinic in Bangladesh and was Chief of Pediatric Infectious Diseases at East Tennessee Children's Hospital.

2023 Science Forum:
Advancing Regulatory Science Through Innovation

AGENDA | Day 1: June 13, 2023

9:00 am – 9:05 am	Introduction Sharron Watson Office of Scientific Professional Development (OSPD), FDA
9:05 am - 9:15 am	Welcome Namandjé N. Bumpus, PhD, Chief Scientist, FDA
9:15 am - 9:30 am	Opening Remarks and Introduction of Keynote Speaker Robert M. Califf, MD, Commissioner, FDA
9:30 am - 10:00 am	Keynote Speaker Murray Lumpkin, MD, Deputy Director of Integrated Development, Bill & Melinda Gates Foundation
10:00 am - 10:30 am	Break

Learning Objectives:

1. Discuss FDA contributions to the evolving science of clinical, non-clinical, and post-market evaluation.
2. Discuss how innovative approaches in evolving areas such as biomarkers, alternative methods for toxicity assessment, precision toxicology prediction, analytical chemistry, and advanced manufacturing may contribute to advances in regulatory decision-making and improve product quality and timeliness.
3. Discuss how FDA leverages social and behavioral sciences to empower patients and consumers.
4. Explain how AI and big data together can improve public health.
5. Discuss scientific advances using the One Health approach to innovative and continuous surveillance of food and cosmetic safety.
6. Discuss FDA's intramural and extramural regulatory science research to support Medical Countermeasure's (MCMs) and emerging technologies to reduce or eliminate pathogens from medical products. The presentations will discuss the application of innovative tools and approaches to support pandemic response, development, and evaluation of MCMs and the detection of emerging agents.
7. Discuss how regenerative medicine and microbiome affect both individual and public health.
8. Describe methods that scientists at FDA are using to study and combat problems associated with substances of abuse.

Concurrent Session 1: Improving Clinical and Post-market Evaluation

Time: 10:30am - 12:30pm

Session Chairs/Moderator: Ruth Barratt, PhD, DVM
FDA Center for Drug Evaluation and Research (CDER)

Time	Presentation	Speaker
10:30am - 10:50am	Clinical Evidence and Medical Devices: Generating Actionable Evidence from the Real World	**Mary Beth Ritchey, PhD** FDA Center for Devices and Radiological Health (CDRH)
10:50am - 11:10am	CDER/CBER Real-world Evidence Program	**John Concato, MD** FDA Center for Drug Evaluation and Research (CDER)
11:10am - 11:30am	Real-world Evidence for Vaccine Effectiveness at FDA Center for Biologics Evaluation and Research	**Richard Forshee, PhD** FDA Center for Biologics Evaluation and Research (CBER)
11:30am - 12:00pm	Real-world Evidence to Provide Supportive Evidence for Evaluating the Safety and Effectiveness of Therapeutic Products	**Sebastian Schneeweiss, MD, ScD** Harvard University
12:00pm - 12:30pm	Panel Discussion and Q&A	**Mary Beth Ritchey, PhD** **John Concato, MD** **Richard Forshee, PhD** **Sebastian Schneeweiss, MD, ScD** **Ruth Barratt, PhD, DVM**

Concurrent Session 2: Product Development Tools and Manufacturing

Time: 10:30am - 12:30pm

Session Chairs/Moderator: Suzanne Fitzpatrick, PhD
FDA Center for Food Safety and Applied Nutrition (CFSAN)

Time	Presentation	Speaker
10:30 am - 11:00 am	Advancing Drug Discovery with Biofabricated 3D Tissue Models	**Marc Ferrer, PhD** NIH National Center for Advancing Translational Sciences (NCATS)
11:00 am - 11:15 am	Advancing Translational Models and Tools into the Drug Review Process: Opportunities for Microphysiological Systems (MPS)	**Kevin Ford, PhD** FDA Center for Drug Evaluation and Research (CDER)
11:15 am - 11:30 am	Opportunities and Challenges in Using Liver Microphysiological Systems to Study Drug Metabolism and Hepatotoxicity	**Qiang Shi, PhD** FDA National Center for Toxicological Research (NCTR)
11:30 am - 11:45 am	Advanced Analytical Methods for Assessing the Efficacy of Regenerative Medicine Cellular Products	**Kyung Sung, PhD** FDA Center for Biologics Evaluation and Research (CBER)
11:45 am - 12:00 pm	Additive Manufacturing: A Case Study in Advanced Manufacturing of Medical Devices	**Matthew Di Prima, PhD** FDA Center for Devices and Radiological Health (CDRH)
12:00 pm - 12:15 pm	Enhancing Regulatory Toxicology Decision-making for Tobacco Products: The Role of Computational Toxicology Tools	**Luis Valerio Jr., PhD** FDA Center for Tobacco Products (CTP)
12:15 pm - 12:30 pm	Panel Discussion and Q&A	**Marc Ferrer, PhD** **Kevin Ford, PhD** **Qiang Shi, PhD** **Kyung, Sung, PhD** **Matthew Di Prima, PhD** **Luis Valerio Jr., PhD** **Suzanne Fitzpatrick, PhD**
12:30 pm - 1:30 pm	Lunch	

Concurrent Session 3: Empowering Patients and Consumers

Time: 1:30pm - 3:30pm

Session Chairs/Moderator: Kathryn LaRosa, MPH
FDA Center for Tobacco Products (CTP)

Time	Presentation	Speaker
1:30 pm - 2:00 pm	Discussion on Increasing the Diversity of Patient and Caregiver Engagement with the Center for Biologics Evaluation and Research on Food Allergy Drug Development	**Joey Mattingly, PharmD, PhD** University of Utah, College of Pharmacys
2:00 pm - 2:15 pm	Providing Information Needed to Make Decisions about COVID-19 Vaccines: Qualitative Testing of Educational Materials	**Alexandria Smith, MSPH** FDA Center for Drug Evaluation and Research (CDER)
2:15 pm - 2:30 pm	Amplifying Equity of Voices: Empowering Patients and Consumers	**Julie Hsieh, PhD** FDA Office of the Commissioner (OC), Office of Minority Health and Health Equity (OMHHE)
2:30 pm - 2:45 pm	FDA's Closer to Zero Initiative: What Parents Can Do to Help Protect Children from Environmental Contaminants	**Kellie Casavale, PhD** FDA Center for Food Safety and Applied Nutrition (CFSAN)
2:45 pm - 3:00 pm	Promoting Antimicrobial Stewardship in the Next Generation: Educational Projects Funded by the FDA's Veterinary Laboratory Investigation and Response Network	**Sarah Peloquin, DVM** FDA Center for Veterinary Medicine (CVM)
3:00 pm - 3:15 pm	A Patient-centered Approach Toward the Development of a Patient-reported Outcome Measure	**Fraser Bocell, PhD** FDA Center for Devices and Radiological Health (CDRH)
3:15 pm - 3:30 pm	Panel Discussion and Q&A	**Joey Mattingly, PharmD, PhD** **Alexandria Smith, MSPH** **Kellie Casavale, PhD** **Sarah Peloquin, DVM** **Fraser Bocell, PhD** **Kathryn LaRosa, MPH** **Julie Hsieh, PhD**

Concurrent Session 4: Tools to Effectively Use Big Data

Time: 1:30pm - 3:30pm

Session Chairs/Moderator: Hesha Duggirala, PhD
FDA Center for Center for Veterinary Medicine (CVM)

Time	Presentation	Speaker
1:30 pm - 2:00 pm	Securing Machine Endpoints in a Post-Quantum Operating Environment	**Jose L. Arrieta** Imagineer
2:00pm - 2:10 pm	Reimagining Regulatory Data Submissions through Fast Healthcare Interoperability Resources (FHIR)	**Jose Galvez, MD** FDA Center for Drug Evaluation and Research (CDER)
2:10pm - 2:20pm	Leveraging Large Datasets for the Development and Evaluation of New Artificial Intelligence (AI)-Enabled Medical Imaging Devices	**Frank Samuelson, PhD** FDA Center for Devices and Radiological Health (CDRH)
2:20pm - 2:30pm	Using Genomic Data and Machine Learning to Study Antimicrobial Resistance in Foodborne Pathogens	**Amy Merrill, MS** *and* **Chih-Hao Hsu, PhD** FDA Center for Veterinary Medicine (CVM)
2:30pm - 2:40pm	Machine Learning and Case Identification in Claims Data	**Ravi Goud, MD** FDA Center for Biologics Evaluation and Research (CBER)
2:40pm - 2:50pm	Using Machine Learning to Predict Non-compliance in the Global Food Supply: Improving Risk-informed Resource Allocation and Public Health Protection	**Jeffrey Chou, MSPH** FDA Center for Food Safety and Applied Nutrition (CFSAN)
2:50pm - 3:30pm	Panel Discussion	**Steve Condrey, MPS** Office of Regulatory Affairs (ORA) **Joshua Xu, PhD** FDA National Center for Toxicological Research (NCTR) **Yu Mei, PhD** FDA Center for , PharmD, PhD (OC/OMHHE)

End of Day 1

2023 Science Forum:
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AGENDA | Day 2: June 14, 2023

Concurrent Session 5: Food and Cosmetic Safety

Time: 9:00am - 11:00am

Session Chairs/Moderator: Rajesh Nayak, PhD (NCTR)

Time	Presentation	Speaker
8:55am-9:00 am	Introduction	**Rokhsareh Shahidzadeh** Office of Scientific Professional Development (OSPD), FDA
9:00am - 9:30am	International Liaison Group for Methods on Risk Assessment of Chemicals (ILMERAC): Sharing Scientific Expertise in the Area of Methodologies for Chemicals in Food with National and International Risk Assessment Agencies across the Globe	**Djien Liem, PhD** European Food Safety Authority (EFSA), Parma, Italy
9:30am - 9:45am	Progress and Needs for New Alternative Methods in CFSAN's Regulatory Mission	**Steven M. Musser, PhD** FDA Center for Food Safety and Applied Nutrition (CFSAN)
9:45am - 10:00am	Studies to Assess the Virulence of Enteric Foodborne Pathogens	**Steven Foley, PhD** FDA National Center for Toxicological Research (NCTR)
10:00am - 10:15am	An Update on NCTR and Office of Cosmetics and Colors' (OCAC) Collaborative Efforts to Support Cosmetics Safety Evaluation	**Luísa Camacho, PhD** FDA National Center for Toxicological Research (NCTR)
10:15am - 10:30am	The US National Antimicrobial Resistance Monitoring System: Helping Ensure the Efficacy of Antibiotics	**Patrick McDermott, PhD** FDA Center for Veterinary Medicine (CVM)
10:30am - 11:00am	Panel Discussion and Q&A	**Djien Liem, PhD** **Steven M. Musser, PhD** **Steven Foley, PhD** **Luísa Camacho, PhD** **Patrick McDermott, PhD** **Rajesh Nayak, PhD**

Concurrent Session 6: Medical Countermeasures, Infectious Disease, and Pathogen Reduction Technologies

Time: 9:00am - 11:00am

Session Chairs/Moderators: Jenna Osborn, PhD (CDRH); Monica (Burts) Young, PhD (CBER); and Mugimane Manjanatha, PhD (NCTR)

Time	Presentation	Speaker
9:00am - 9:05am	Introduction	**Mugimane Manjanatha, PhD** FDA National Center for Toxicological Research (NCTR)
9:05am - 9:25am	Investing in the Future of Health Security	**Sandeep Patel, PhD** Biomedical Advanced Research and Development Authority (BARDA)
9:25am - 9:45am	FDA ARGOS: Where Trusted Sequence Data Meets Quality by Design Approach	**Vahan Simonyan, PhD, DSc** Embleema and George Washington University
9:45am - 10:00am	Assessing the Role of T-cell Responses in SARS-CoV-2 Protection	**Marian Major, PhD** FDA Center for Biologics Evaluation and Research (CBER)
10:00am - 10:15am	Development of Regulatory Science Tools to Accelerate Development of Medical Devices in Public Health Emergencies	**Jenna Osborn, PhD** FDA Center for Devices and Radiological Health (CDRH)
10:15am - 10:30am	Development of a Platform Approach to Model Neurotropic Viral Infections and Characterize the Therapeutics that Target Them	**Daniela Verthelyi, MD, PhD** FDA Center for Drug Evaluation and Research (CDER)
10:30am - 10:45am	Evaluation of Testicular Organoids as a Model for Zika Virus Infection	**Dayton Petibone, PhD** FDA National Center for Toxicological Research (NCTR)
10:45am - 11:00am	Panel Discussion and Q&A	**Mugimane Manjanatha, PhD** **Sandeep Patel, PhD** **Vahan Simonyan, PhD, DSc** **Marian Major, PhD** **Jenna Osborn, PhD** **Daniela Verthelyi, MD, PhD** **Dayton Petibone, PhD**
11:00 am - 12:00	Lunch	

Concurrent Session 7: Advancing Products Based on Novel Technologies

Time: 12:00pm - 2:00pm

Session Chairs/Moderators: Julie Schneider, PhD
FDA Oncology Center of Excellence (OCE); and
Mugimane Manjanatha, PhD (NCTR)

Time	Presentation	Speaker
12:00 pm – 12:30 pm	Update on Personalized Cancer Vaccines	**Catherine J. Wu, MD** Dana-Farber Cancer Institute and Harvard Medical School
12:30pm - 12:45pm	Use of Next Generation Sequencing (NGS) technologies in B-cell Receptor-Based Immunome Profiling and Minimal Residual Disease (MRD) Biomarker Discovery	**Wenming Xiao, PhD** FDA Center for Drug Evaluation and Research (CDER)
12:45pm - 1:00pm	Host-Microbiome Crosstalk: Disruption of Gastrointestinal Barrier as Toxicity Assessment Tool	**Sangeeta Khare, PhD** FDA National Center for Toxicological Research (NCTR)
1:00pm - 1:15pm	Regulatory Perspectives on Advancing Regenerative Medicine Products and Emerging Technologies	**Carolyn Yong, PhD** FDA Center for Biologics Evaluation and Research (CBER)
1:15pm - 1:30pm	Dermal Drug Delivery via Dissolvable Microneedles: Formulation Variables Affecting Critical Quality Attributes (CQAs)	**Nahid Kamal, PhD** FDA Center for Drug Evaluation and Research (CDER)
1:30pm - 1:45pm	Assessment of Trabecular Bone Stiffness Using Radiomics and Deep-learning Features	**Qian Cao, PhD** FDA Center for Devices and Radiological Health (CDRH)
1:45 pm – 2:00 pm	Panel Discussion and Q&A	**Catherine J. Wu, MD** **Wenming Xiao, PhD** **Sangeeta Khare, PhD** **Carolyn Yong, PhD** **Nahid Kamal, PhD** **Qian Cao, PhD** **Mugimane Manjantha, PhD**

Concurrent Session 8: Substance Use, Misuse, and Addiction

Time: 12:00pm - 2:00pm

Session Chairs/Moderators: Arit Harvanko, PhD
FDA Center for Tobacco Products (CTP)

Time	Presentation	Speaker
12:00 pm – 12:05 pm	Introduction	**Marta Sokolowska, PhD** FDA Center for Drug Evaluation and Research (CDER)
12:05 pm – 12:35 pm	Abuse Liability Testing with Humans: Review of Standard Methods and Recent Innovations Using Cigarettes Varying in Nicotine Content as an Exemplar	**Stephen T. Higgins, PhD** University of Vermont
12:35 pm – 12:45 pm	Field Deployable Analytical Toolkit for Rapid Analysis of FDA-Regulated Products at International Ports of Entry	**LT Martin M. Kimani, PhD** Office of Regulatory Affairs (ORA)
12:45pm - 12:55pm	Blunt and Non-Blunt Cannabis Use Associated with Cigarette, E-Cigarette, and Cigar Initiation: Findings from the Population Assessment of Tobacco and Health Study	**Heather L. Kimmel, PhD** NIH National Institute on Drug Abuse (NIDA)
12:55pm - 1:05pm	Leveraging Systems Modeling to Inform Policies on Opioids	**Sara Eggers, PhD** FDA Center for Drug Evaluation and Research (CDER)
1:05pm - 1:15pm	Public Health Harms from Prescription Stimulant Diversion and Nonmedical Use	**Rose Radin, PhD** FDA Center for Drug Evaluation and Research (CDER)
1:15pm - 1:25pm	Barriers to Prescribing Buprenorphine as a Medication for Opioid Use Disorder: Healthcare Providers' Practices, Perspective, and Experiences	**Matthew Walker, DrPH** FDA Center for Drug Evaluation and Research (CDER)
1:25pm - 1:35pm	Neonatal Opioid Withdrawal Syndrome: A Scientific and Regulatory Update	**An Massaro, MD** FDA Office of the Commissioner (OC)

continued

1:35pm - 2:00pm	Panel Discussion	Marta Sokolowska, PhD Stephen T. Higgins, PhD LT Martin M. Kimani, PhD Heather L. Kimmel, PhD Sara Eggers, PhD Rose Radin, PhD Matthew Walker, DrPH An Massaro, MD Arit Havanko, PhD

End of Day 2

Speaker Bios and Abstracts

Concurrent Session 1: Improving Clinical and Post-market Evaluation

Clinical Evidence and Medical Devices: Generating Actionable Evidence from the Real World

Mary Beth Ritchey, PhD, MSPH, FISPE

Chief Epidemiologist, Office of Clinical Evidence and Analysis
FDA, Center for Devices and Radiological Health

Mary Beth Ritchey, PhD, MSPH, FISPE, has spent her career dedicated to better understanding medical product safety and effectiveness in actual clinical practice. She has worked in government, industry, consulting, and academia, and she uses this experience to advocate for generating and interpreting clinical evidence that is meaningful to all stakeholders in this space.

As the Chief Epidemiologist for the Center for Devices and Radiological Health, Dr. Ritchey provides technical and scientific leadership on study designs using real-world data (RWD), execution, and interpretation of results for specific studies. She also provides guidance, expertise, direction, and feedback related to clinical evidence and RWD-specific policy and programs. She holds bachelor's degrees in chemistry (Duke University) and nursing (University of North Carolina [UNC] at Chapel Hill), along with master's and doctoral degrees in epidemiology from the UNC Gillings School of Global Public Health.

Abstract: Clinical Evidence and Medical Devices: Generating Actionable Evidence from the Real World

Per medical device regulations, FDA relies only upon valid scientific evidence to determine whether there is reasonable assurance that the device is safe and effective. This presentation will describe considerations for clinical studies generally, to generate valid scientific evidence, then further extend these concepts to assessment of relevance and reliability for clinical studies using RWD. Therapeutic device and digital health examples will be provided, with a focus on the following aspects of studies using RWD: study design and analysis; defining the study population and data elements; completion, accuracy, and timeliness of data; and human subjects protections. Major obstacles (e.g., identifying devices in the absence of structured identifiers in many data sources) and unique opportunities (e.g., integration of patient generated health data) for devices will be highlighted.

CDER/CBER Real-world Evidence Program

John Concato, MD, MS, MPH

Associate Director, Real-world Evidence Analytics,
Office of Medical Policy
FDA, Center for Drug Evaluation and Research

John Concato, MD, MS, MPH, is Associate Director for Real-world Evidence Analytics in FDA's Office of Medical Policy at the Center for Drug Evaluation and Research. His responsibilities focus on FDA's Real-world Evidence (RWE) Program and include internal agency processes, external stakeholder interaction, demonstration projects, and guidance development; he also chairs DA's RWE Subcommittee. Dr. Concato joined FDA after a 27-year career at the Yale University School of Medicine and the Department of Veterans Affairs, where he was a Professor of Medicine, Director of the Veterans Affairs' (VA) Clinical Epidemiology Research Center, and one of two founding principal investigators of the VA Million Veteran Program genomic mega-biobank.

His peer-review publications include Randomized, Controlled Trials, Observational Studies, and the Hierarchy of Research Designs (2000); Million Veteran Program: A Mega-Biobank to Study Genetic Influences on Health and Disease (2016); Real-world Evidence — What's in a Name? (2020); and Real-world Evidence — Where Are We Now? (2022). Dr. Concato received a BE degree from the Cooper Union, MD and MS degrees from New York University, and an MPH degree from Yale University.

Abstract: CDER/CBER Real-world Evidence Program

The evidentiary standard used by FDA to assess the effectiveness of drugs and other medical products was developed based mainly for evidence obtained from clinical trials. In 2016, the 21st Century Cures Act mandated that FDA evaluate the use of real-world evidence (RWE) to help support approval of a new indication for an already approved drug or to help support post-approval study requirements. RWE is clinical evidence regarding the usage and potential benefits and risks of a medical product derived from analysis of real-world data (RWD). In this context, RWD are data relating to patient health status and/or delivery of health care routinely collected from a variety of sources.

This presentation will provide an overview of the Real-world Evidence Program coordinated by FDA's Center for Drug Evaluation and Research. The focus will be on FDA draft guidance published in support of the 21st Century Cures Act and the Prescription Drug User Fee Act VII. Other guidance documents, as well as research projects evaluating the use of real-world evidence, will also be discussed.

Real-world Evidence for Vaccine Effectiveness at FDA's Center for Biologics Evaluation and Research

Richard Forshee, PhD

Deputy Director, Office of Biostatistics and Pharmacovigilance
FDA, Center for Biologics Evaluation and Research

Richard Forshee, PhD, is the Deputy Director of the Office for Biostatistics and Pharmacovigilance (OBPV) at FDA's Center for Biologics Evaluation and Research (CBER). He has more than 25 years of experience as a researcher and leader in academia and FDA. He joined FDA full time in 2008 after working for more than a decade in academia. At FDA, he led the Analytics and Benefit-Risk Assessment Team for OBPV in CBER and worked extensively to provide quantitative benefit-risk assessment, health informatics, and real-world evidence to ensure the safety and efficacy of biologic products. This work supports OBPV's review, regulatory, and public health missions. Dr. Forshee provides knowledge and expertise on scientific and regulatory matters at Center, Agency, US government, and international meetings, workshops, and conferences.

Dr. Forshee has won numerous awards, including the FDA Award of Merit, the FDA-CBER Award for Managerial Excellence, and the CBER Hope Hopps Memorial Award. In 2020, he received the Society for Risk Analysis Outstanding Practitioner Award. He has published more than 100 scientific articles, which have been cited more than 4,000 times.

Abstract: Real-world Evidence for Vaccine Effectiveness at FDA's Center for Biologics Evaluation and Research

FDA's Center for Biologics Evaluation and Research has been building our capability to work with real-world evidence (RWE) for many years. Much of the work has focused on studies of vaccine effectiveness. This presentation will review several studies that have applied innovative methods to detect and/or minimize bias in an analysis. These methods include efforts to make cohorts comparable on measured variables, using negative controls, and using linked external datasets to check for balance on unmeasured variables.

Real-world Evidence as a Means to Provide Supportive Evidence for Evaluating the Safety and Effectiveness of Therapeutic Products

Sebastian Schneeweiss, MD, ScD

Professor of Medicine and Epidemiology, Harvard Medical School
Division Chief, Pharmacoepidemiology, Department of Medicine, Brigham and Women's Hospital

Sebastian Schneeweiss, MD, ScD, focuses his research on assessing the effectiveness and safety of biopharmaceuticals in clinical practice. He has developed and applied analytic methods to improve the accuracy of estimating causal treatment effects of new drugs using complex digital health-care databases. His work has been published in more than 500 articles and is used for regulatory and coverage decision-making around the globe. He is funded by the National Institutes of Health, the Patient-centered Outcomes Research Institute, the Burroughs Wellcome Fund, and FDA. He is Principal Investigator of FDA's Sentinel Innovation Center and co-leads the RCT-DUPLICATE (Randomized, Controlled Trials Duplicated Using Prospective Longitudinal Insurance Claims: Applying Techniques of Epidemiology) initiative and ENCORE to understand when and how real-world evidence studies can reach robust conclusions to support regulatory and health-technology-assessment submissions. He is Past President of the International Society for Pharmacoepidemiology and is a Fellow of the American College of Epidemiology, the American College of Clinical Pharmacology, and the International Society for Pharmacoepidemiology.

Abstract: Real-world Evidence As a Means to Provide Supportive Evidence for Evaluating the Safety and Effectiveness of Therapeutic Products

Regulatory agencies across the world increasingly consider real-world evidence (RWE) for effectiveness claims in medical product approval and coverage decisions. RWE complements randomized-controlled-trial evidence to understand the effectiveness and safety of medical products in clinical practice by analyzing large longitudinal health-care data. In order to support decision-makers, we need (1) full transparency of study implementation, (2) fit-for-purpose data, (3) causal study designs and analyses, and (4) approaches that facilitate the review of RWE studies. This talk illustrates advances in these areas, with empirical examples and recent regulatory developments.

Moderator

Ruth Barratt, PhD DVM

Senior Science Advisor
FDA, Center for Drug Evaluation and Research

Dr. Barratt has worked in industry and in two different review divisions at FDA's Center for Veterinary Medicine providing expert consults on immunology and immunotoxicity issues, subject matter expertise on enterprise application development for reviews, and human food safety health hazard and risk assessments. In 2008, she moved to the Center for Drug Evaluation and Research (CDER) in the Office of Translational Sciences.

In her current position, Ruth has initiated and led various center regulatory science initiatives to build programs and processes to grow CDER's research portfolio and reported on CDER's research portfolio to garner support for research funding. Her efforts help formulate strategies for the center's research activities supporting the evaluation and approval of human drugs. Using her knowledge of CDER's diverse research portfolio and management, she mentors CDER's research community to promote successful outcomes for regulatory science. Ruth serves as a CDER representative in the wider FDA community on research needs and policy.

Speaker Bios and Abstracts

Concurrent Session 2: Product Development Tools and Manufacturing

Advancing Drug Discovery with Biofabricated 3D Tissue Models

Marc Ferrer, PhD

Director, 3D Tissue Bioprinting Laboratory
NIH, National Center for Advancing Translational Sciences

Marc Ferrer, PhD, is the Director of the National Center for Advancing Translational Sciences' (NCATS) 3D Tissue Bioprinting Laboratory, a multidisciplinary lab with the goal of developing, validating, and using bioengineered 3D tissues for disease modeling and drug discovery and development. Previously, Dr. Ferrer was a Team Lead at the National Institutes of Health's Chemical Genomics Center, where he worked on the discovery of small molecule probes to study protein function. Before joining NIH, he was Director of Assay Development and High Throughput Screening at the Department of Automated Biotechnology at the Merck Research Laboratories. Dr. Ferrer received his BSc degree in Organic Chemistry from the University of Barcelona, and his PhD degree in Biological Chemistry from the University of Minnesota.

Abstract: Advancing Drug Discovery with Biofabricated 3D Tissue Models

3D tissue models are being developed as predictive efficacy and toxicity assays in early drug discovery and preclinical development. This presentation will discuss work at the National Center for Advancing Translational Sciences' 3D Tissue Bioprinting Laboratory (3DTBL) to create and operationalize a platform of biofabricated 3D tissue models with relevant functional assay readouts to accelerate the discovery and development of therapeutics. The 3DTBL uses human induced pluripotent stem-cells-derived and primary cells, tissue engineering technologies, including bioprinting and tissue chips, to establish a portfolio of biologically validated healthy and disease 3D tissue models of increased physiological complexity as needed to mimic different tissue and organ physiologies and disease pathologies. This presentation will describe examples of the approaches used at the 3DTBL for the versatile and robust production of engineered 3D tissues in multi-well high throughput plate format and their use for disease modeling and compound testing.

Advancing Translational Models and Tools into the Drug Review Process: Opportunities for MPS

Kevin Ford, PhD, DABT, DSP

Associate Director, Division of Applied Regulatory Science
FDA, Center for Drug Evaluation and Research

Kevin Ford, PhD, DABT, DSP, is a board-certified toxicologist and safety pharmacologist, with drug development and leadership experience in the pharmaceutical and biotechnology industry. Dr. Ford joined FDA in 2021 and is currently an Associate Director in the Division of Applied Regulatory Science (DARS). In DARS, Dr. Ford supervises scientists in the areas of microphysiological systems, electrophysiology, drug metabolism and computational toxicology. Before joining FDA, Dr. Ford served as the Associate Director of Toxicology at Global Blood Therapeutics. Previously, he worked for 10 years at Genentech, where he held different positions and was involved with drug development programs across diverse therapeutic areas. Dr. Ford has substantial expertise in computational toxicology and pharmacology, pharmacokinetics, and metabolism, and the development and use of novel methodologies to assess biomarkers and advance novel drug development tools. Dr. Ford earned his PhD in Molecular Toxicology from the University of California, Berkeley, and completed a postdoctoral fellowship at the Massachusetts Institute of Technology.

Abstract: Advancing Translational Models and Tools into the Drug Review Process: Opportunities for MPS

Microphysiological systems (MPS) have gained considerable attention in recent years as promising in vitro tools to recapitulate human physiology by recreating key biological processes and cellular architecture. MPS has proven to be a reliable tool in the drug development process for the investigation of safety assessment; absorption, distribution, metabolism, and excretion; and pharmacokinetics. MPS have become an integral part of the drug development process by many pharmaceutical companies, in part due to (1) the continuous rising costs of developing new drugs, (2) the drive to reduce animal experimentation, and (3) the need for more predictive and high-throughput in vitro models. This presentation will highlight some of the applied MPS research being performed at the Division of Applied Regulatory Science (DARS) in the Center for Drug Evaluation and Research (CDER) at FDA. A discussion of the performance and application of several of the MPS models used in DARS (liver, lung, gut, and heart) will also be provided.

Opportunities and Challenges in Using Liver Microphysiological Systems to Study Drug Metabolism and Hepatotoxicity

Qiang Shi, PhD
Visiting Scientist
FDA, National Center for Toxicological Research

Qiang Shi, PhD, holds a doctorate in pharmacology from Zhejiang University in China. He completed his postdoctoral training in drug-induced liver injury (DILI) at FDA's National Center for Toxicological Research between 2007 and 2010, where he became a Visiting Scientist. Dr. Shi's main research focus is mechanisms, biomarkers, and models for DILI. He has more than 20 years of experience in the culture of primary hepatocytes from multiple species, with a mechanistic focus on drug-induced mitochondrial damage and metabolism-mediated hepatocyte injury. Dr. Shi's most recent work involves the study of DILI induced by FDA-approved small-molecule kinase inhibitors and the use of liver-on-a-chip for liver adaptation in response to DILI.

Abstract: Opportunities and Challenges in Using Liver Microphysiological Systems to Study Drug Metabolism and Hepatotoxicity

Liver microphysiological systems (MPS) are designed to better preserve the functions of in vitro cultured hepatic cells and are emerging as novel tools for the study of drug metabolism and hepatotoxicity. Many types of liver MPS have been published, and some have been recently commercialized. Evidence is accumulating that liver MPS may improve the accuracy in predicting drug hepatotoxicity and metabolism as compared to conventional cell culture, though most findings have not been confirmed by independent studies. Guidelines have been proposed to develop and evaluate liver MPS for possible regulatory use. The challenges, like lack of standardized protocols for toxicity and functional assays and cell qualification, will also be discussed.

Advanced Analytical Methods for Assessing the Efficacy of Regenerative Medicine Cellular Products

Kyung, Sung, PhD

Acting Chief, Cellular and Tissue Therapies Branch, Office of Cellular Therapy and Human Tissue
FDA, Center for Biologics Evaluation and Research

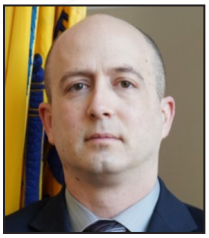
Kyung Sung, PhD, is the Acting Chief of the Cellular and Tissue Therapy Branch in the Office of Cellular Therapy and Human Tissue in the Center for Biologics Evaluation and Research. Her research focuses on developing new quantitative assays using various biomedical engineering tools to study the impact of interactions between living cells and biomaterials used in the manufacture and characterization of regenerative medicine cellular products. She received her PhD in Chemical Engineering from the University of Michigan, Ann Arbor, and did her postdoctoral training at the University of Wisconsin, Madison. She also worked as a patent examiner in Biotechnology at the Patent and Trademark Office before she joined FDA in 2015.

Abstract: Advanced analytical methods for assessing the efficacy of regenerative medicine cellular products

Multipotent stromal cells (MSCs) have become popular sources for manufacturing regenerative medicine cellular products, due to their ability to undergo lineage-specific differentiation. MSCs, on the other hand, are heterogeneous and responsive to their surroundings, resulting in distinct subpopulations of cells with potentially different properties required for product potency. Because there are numerous biochemical and biomechanical factors that influence MSC function, developing reliable, high-throughput assays that allow for the efficient exploration of large and complex parameters for evaluating cellular function is critical.

Microphysiological systems offer a viable solution to this unmet need. This presentation will provide an overview of regenerative medicine cellular product regulation as well as easy-to-use, microscale technologies that improve throughput, relevance, and reliability. How such technologies could be used to evaluate the efficacy of regenerative medicine cellular products will be discussed.

Additive Manufacturing: A Case Study in Advanced Manufacturing of Medical Devices



Matthew Di Prima, PhD

Materials Engineer
FDA, Center for Devices and Radiological Health

Matthew Di Prima, PhD, received his doctorate in Materials Science and Engineering from the Georgia Institute of Technology. Since 2010, he has been working as research materials scientist at the Center for Devices and Radiological Health (CDRH) in FDA. His areas of research are investigating how the additive manufacturing process can affect device performance and the interplay between corrosion and durability testing. Along with his research duties, he is the Co-Chair of the Advanced Manufacturing Technologies Working Group, which is spearheading efforts across FDA to address how advanced manufacturing technologies affects regulated medical products, as well as the Chair of the CDRH Additive Manufacturing Working Group, which leads efforts across CDHR on how additive manufacturing affects medical device performance. These efforts include guidance and standards development, device review harmonization, and performing regulatory science, with the intent to foster innovative and high-quality products while maintaining they have the same safety and effectiveness Americans have come to expect. He is also active in standards development and is Co-Chair of American Society for Testing and Materials F42.07.03, Additive Manufacturing Applications: Medical/Biological.

Abstract: Additive Manufacturing: A Case Study in Advanced Manufacturing of Medical Devices

"Additive Manufacturing" (AM) is a blanket term for a suite of manufacturing technologies that use a digital format to build a part layer by layer. While this technology was developed in the early 1980s and commercialized later that decade, it saw little use in medical device production before 2000. From 2010 to 2020, the Center for Devices and Radiological Health (CDRH) stood up a working group focused on AM, had significant stakeholder interactions, published a Guidance, and assumed leadership in AM standards development. As a result, the handful of 510(k) cleared devices utilizing AM technologies in 2010 jumped to over 250 by 2020. To work through this process, the medically relevant AM technologies will be discussed, along with the perceived benefits of using AM for medical device production. Then, the kinds of 510(k) cleared devices and observed trends in those clearances will be presented from that decade, along with the concurrent standards in development. The presentation will conclude with CDRH's activities across that decade to ensure AM device safety and effectiveness.

Enhancing Regulatory Toxicology Decision-making for Tobacco Products: The Role of Computational Toxicology Tools

Luis Valerio Jr., PhD, ATS

Associate Director, Division of Nonclinical Science, Office of Science
FDA, Center for Tobacco Products (CTP)

Luis Valerio Jr., PhD, ATS, is Associate Director of the Division of Nonclinical Science in the Office of Science (OS) at FDA's Center for Tobacco Products (CTP). He has been with FDA for 19 years, reviewing regulated products and applied research at the Center for Food Safety and Applied Nutrition, the Center for Drug Evaluation and Research, and CTP. He has leadership experience in the private sector in chemical safety and risk assessment and is a board-certified toxicologist. He represents CTP in FDA's Alternative Methods Working Group, which aims to advance and catalyze the development and potential application of new approach methodologies to support regulatory toxicology at the agency. He has led regulatory reviews of electronic nicotine delivery systems at FDA/CTP/OS and has fostered applied research in the area of computational (in silico) toxicology to evaluate chemical constituents present in or emitted by tobacco products. His academic background is in biochemical metabolism and molecular toxicology as a National Research Council Gastroenterology Fellow at the University of Colorado School of Medicine. His PhD is in Pharmaceutical Science from the University of Colorado.

Abstract: Enhancing Regulatory Toxicology Decision-making for Tobacco Products: The Role of Computational Toxicology Tools

Computational models are science-based tools showing promise to enhance the quality of regulatory toxicology evaluations of tobacco products. At the Center for Tobacco Products (CTP), these tools have been evaluated to identify respiratory hazards and predict the genetic toxicity and carcinogenic potential of chemicals found in or emitted by tobacco products. Targeted research by CTP's Office of Science (OS), Division of Nonclinical Science (DNCS), has been conducted and published to understand the utility and performance of these tools as applied to chemicals in tobacco products. In these studies, rigorous validation tests and considerations of mode of action have shown the skill of model predictions and correlation with known experimental toxicity outcomes.

This presentation will discuss DNCS toxicology research and evaluations by the DNCS Nonclinical Computational Toxicology Program, which suggest the role computational toxicology tools may have in supporting chemical-hazard assessments and risk mitigation of tobacco products. Information about data mining, chemical screening, and good practices for use of prediction models to assess toxicities associated with tobacco products will be highlighted. In conclusion, CTP/OS/DNCS is interested in computational toxicology approaches, when appropriate, to enhance the quality of regulatory toxicology evaluations of chemicals found in or emitted by tobacco products.

Speaker Bios and Abstracts

Concurrent Session 3: Empowering Patients and Consumers

Discussion on Increasing the Diversity of Patient and Caregiver Engagement with the Center for Biologics Evaluation and Research on Food Allergy Drug Development

Joey Mattingly, PharmD, MBA, PhD

Associate Professor and Vice Chair of Research,
Department of Pharmacotherapy
University of Utah College of Pharmacy

Joey Mattingly, PharmD, MBA, PhD, is an Associate Professor and Vice Chair of Research in the Department of Pharmacotherapy at the University of Utah College of Pharmacy. Dr. Mattingly has developed a research portfolio that primarily focuses on pharmaceutical policy, where he has engaged policymakers at local, state, and federal levels on topics related to drug pricing, patient engagement, and comparative effectiveness research. In 2022, he was appointed as an advisor to the Center of Medicare and Medicaid Services to aid in the implementation of the new Drug Price Negotiation Program authorized by Congress through the Inflation Reduction Act. Over the past year, he has co-led a large cooperative agreement with FDA (U01FD007563) focused on improving diversity in clinical trials, and he serves as an advisory panel member for Clinical Effectiveness and Decision Science for the Patient-centered Outcomes Research Institute.

Abstract: Discussion on Increasing the Diversity of Patient and Caregiver Engagement with the Center for Biologics Evaluation and Research on Food Allergy Drug Development

To better understand patient and caregiver engagement with FDA and the diversity of individuals providing input on a therapeutic area involving a drug product regulated by the Center for Biologics Evaluation and Research, the Maryland Center of Excellence in Regulatory Science and Innovation conducted a literature review, environmental scan, in-depth interviews, and a public meeting for patients and caregivers impacted by food allergy. From this work, we identified factors that motivated patients and caregivers to engage with FDA as well as potential challenges or barriers for engagement for different groups of patients. Motivating factors included improving food labeling and food-making processes, educating self and others, having a sense of community, increasing representativeness, and having an interest in sharing personal experiences. Barriers for different groups included factors related to cost, travel, time, lack of awareness, and perceived relevance or usefulness. Based on feedback from patients, caregivers, and food allergy advocacy groups, we have identified several opportunities for FDA to improve engagement with this community that may empower different groups to be more involved in FDA's patient engagement activities.

Providing Information Needed to Make Decisions about COVID-19 Vaccines: Qualitative Testing of Educational Materials

Alexandria Smith, MSPH

Social Scientist
FDA, Center for Drug Evaluation and Research

Alexandria Smith, MSPH, is a social scientist with expertise in health communication research and public education campaign evaluation. She is involved with conducting qualitative, quantitative, and mixed-methods social and behavioral science research studies about human drug products. These include projects related to biosimilars, opioids, and other controlled and abusable substances. Prior to joining CDER, she was a social scientist for FDA's Center for Tobacco Products, where she focused on qualitative and quantitative research on youth prevention programs. She received her MSPH from the Johns Hopkins Bloomberg School of Public Health.

Abstract: Providing Information Needed to Make Decisions about COVID-19 Vaccines: Qualitative Testing of Educational Materials

After FDA approved COVID-19 vaccines for youths ages 5-11 and 12-15 and those over age 16, the agency needed to find effective communication strategies for providing information answering pertinent questions about them. To accomplish this, the agency developed a series of educational materials to inform patients' and parents' decision-making about vaccine effectiveness, development, risks and benefits, route of administration, booster eligibility, and corrections to common misperceptions.

Amplifying Equity of Voices: Empowering Patients and Consumers

Julie Hsieh, PhD, MPH

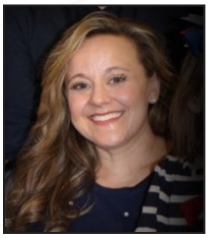
Staff Fellow
FDA, The Office of Minority Health and Health Equity

Julie Hsieh, PhD, MPH, works in FDA's Office of Minority Health and Health Equity (OMHHE), in the Office of the Commissioner, to support the Research and Collaboration Program. She is trained as an infectious disease epidemiologist and has a profound interest in developing and identifying strategies to improve public health among vulnerable populations. Dr. Hsieh has conducted studies of the incarcerated affected by both opioid and HIV/AIDS in the United States and Asia, including ethnic minority populations in rural China, which examined the intersections between their behaviors and the influences on their health. Prior to joining OMHHE, she participated in multiple projects, including conducting research to determine whether the clinical trials population reflects the disease population in the United States by age, sex, race, and ethnicity. Dr. Hsieh received her PhD in Epidemiology from the University of California, Los Angeles, and her MPH from Yale University.

Abstract: Amplifying Equity of Voices: Empowering Patients and Consumers

The Office of Minority Health and Health Equity (OMHHE) launched the Enhance Equity Initiative to support research projects and communication efforts to enhance: EQUITY in clinical trials; EQUITABLE data efforts; and EQUITY of voices. In this session, you will learn how OMHHE amplifies Equity of Voices by learning more about OMHHE's diverse stakeholder community, OMHHE-funded research to leverage novel and big data sources to understand diverse patient perspectives, preferences, and unmet needs, and OMMHE's efforts to expand culturally and linguistically tailored health education (e.g., patient, health care provider).

FDA's Closer to Zero Initiative: What Parents Can Do to Help Protect Children from Environmental Contaminants



Kellie Casavale, PhD, RD

Senior Science Advisor for Nutrition
FDA, Center for Food Safety and Applied Nutrition

Kellie Casavale, PhD, RD, is the Senior Science Advisor for Nutrition in the Office of Analytics and Outreach in FDA's Center for Food Safety and Applied Nutrition. She supports cross-Center and cross-Departmental collaborations, particularly those related to the Dietary Guidelines for Americans (DGAs), Closer to Zero, and maternal and child populations. She has led in the Dietary Guidelines process through roles at the Center for Nutrition Policy and Promotion (within the Department of Agriculture), the Office of Disease Prevention and Health Promotion (within the Department of Health and Human Services), and now FDA for four cycles of the DGAs. She supported the development of the first Dietary Patterns for children under two years with 2020 Dietary Guidelines Advisory Committee. Other leadership roles include serving with the Federal Data Consortium on Pregnancy and Birth to 24 Months, the Human Milk Composition Initiative in the US and Canada, and maternal and child health projects in the Centers for Disease Control and Prevention's National Health and Nutrition Examination Surveys. She contributes leadership for Closer to Zero and the FDA/Environmental Protection Agency's Fish Advice, elucidating the ways nutrition can reduce the adverse developmental effects of potential exposures to environmental chemical contaminants from food.

Abstract: FDA's Closer to Zero Initiative: What Parents Can Do to Help Protect Children from Environmental Contaminants

FDA's Closer to Zero initiative takes a whole-of-government approach to reduce the exposure of young children to environmental contaminants, like heavy metals, from foods, and to educate caregivers on the important roles of food variety and nutrition in helping to protect developing children from the potential adverse health effects associated with environmental contaminants. This food safety issue is multifaceted and complex. Food sources of contaminants can also be sources of nutrients essential for child growth and development and include many foods that are part of healthy dietary pattern recommendations of the Dietary Guidelines for Americans. In addition, these contaminants are in the environment where food is grown or raised and removing them from the environment completely is likely not possible. Attention to this issue, therefore, could have unintended consequences such as parents avoiding foods that are nutritious because they hear the foods are a focus for contaminant reductions. To address these and other challenges, FDA is developing an education strategy, supported by social science research and risk communication theory, to create messages that not only educate and resonate with the public and are grounded in science, but also provide meaningful actions that parents, caregivers, and health professionals can take to support healthy and safe food decisions for families of young children.

Promoting Antimicrobial Stewardship in the Next Generation: Educational Projects Funded by FDA's Veterinary Laboratory Investigation and Response Network

Sarah Peloquin, DVM

Veterinary Medical Officer
FDA, Center for Veterinary Medicine

Sarah Peloquin, DVM, received her BS in Biology, with a secondary emphasis in English, from Juniata College in 2011. She then received her DVM from Virginia-Maryland College of Veterinary Medicine in 2015. Upon graduation from veterinary school, Dr. Peloquin worked in private practice as a small-animal veterinarian for three years. She joined FDA's Center for Veterinary Medicine in 2018.

Dr. Peloquin is currently a Veterinary Medical Officer for the Veterinary Laboratory Investigation and Response Network (Vet-LIRN) in the Office of Applied Science, where she leads outreach and antimicrobial resistance stewardship efforts. She is also actively involved in One Health committee work and supports Vet-LIRN's response to consumer complaints reporting potential illness in animals.

Promoting Antimicrobial Stewardship in the Next Generation: Educational Projects Funded by FDA's Veterinary Laboratory Investigation and Response Network

In recent years, antimicrobial resistance (AMR) has become an imminent threat to both humans and animals. Because veterinary use of antimicrobials can have a direct impact on the development of AMR, FDA's Center for Veterinary Medicine (CVM) created a five-year Veterinary Stewardship Action Plan in 2019. One of the primary goals of the initiative is to support antimicrobial stewardship in veterinary settings.

In particular, CVM's Veterinary Laboratory Investigation and Response Network (Vet-LIRN) contributes to this goal by providing funding to veterinary academic institutions to support antimicrobial stewardship. Vet-LIRN coordinates a network of 46 veterinary diagnostic laboratories across the United States and Canada, and most of these laboratories are located at veterinary schools. By leveraging its existing relationships with veterinary schools, Vet-LIRN is in a unique position to provide funding for the development of educational materials on AMR stewardship.

Since 2020, Vet-LIRN has funded seven grants to five veterinary schools. The seven projects vary in their scope, but all have a common goal of promoting antimicrobial stewardship, including improving access to antimicrobial susceptibility testing, developing stewardship plans, and educating animal owners, veterinary students, and veterinarians. Educating future generations of veterinarians on the importance of using antimicrobials appropriately will play a vital role in the global fight against AMR.

A Patient-Centered Approach toward the Development of a Patient-reported Outcome Measure

Fraser D. Bocell, PhD, Med

Social Scientist and Psychometrician
FDA, Center for Devices and Radiological Health

Fraser D. Bocell, PhD, Med, is a Psychometrician and Clinical Outcome Assessment Reviewer with the Patient Science and Engagement Team in FDA's Center for Devices and Radiological Health (CDRH). At CDRH, he provides expertise and training, leads patient-centered research, and helps develop policy on the evaluation and use of clinical outcome assessments in regulatory decision-making. His recent research has focused on the use of patient-reported outcome measures (PROM) in device submissions and focus groups involving patients with temporomandibular joint disease, as well as focus groups to understand the impact of profound vision loss. His work helps bring patient voices to regulatory decision-making.

Abstract: A Patient-Centered Approach toward the Development of a Patient-reported Outcome Measure

Patients are the experts on the symptoms they experience due to their condition. Understanding symptoms of temporomandibular joint disorders (TMDs) can help doctors and patients document, monitor, and manage the disease and help researchers evaluate interventions. Patients with TMDs experience symptoms ranging from mild to severe, primarily in the head and neck region. This study describes findings from formative patient focus groups to capture, categorize, and prioritize symptoms of TMDs toward the development of a patient-reported outcome measure.

Moderator

Kathryn LaRosa, MPH

Program Analyst, Office of Science
FDA, Center for Tobacco Products

Kathryn LaRosa, MPH, serves as a program analyst for FDA's Office of Science in the Center for Tobacco Products. She specializes in administrative practices and is responsible for maintaining and organizing various projects across the Research Operations and Advisory Resources branch, including assisting in scientific conference management, and supporting her team with interagency collaborations relating to research. LaRosa received her MPH from George Mason University.

Securing Machine Endpoints in a Post-quantum Operating Environment

Jose Arrieta

Chief Executive Officer, Imagineer

Jose Arrieta is the former Chief Information Officer and Chief Data Officer of the Department of Health and Human Services (HHS). He oversaw $6.3B in IT investments, $800B in grants, and $26B in federal contracts in his last three years at HHS. He provided cybersecurity solutions for 174,000 people and a network that transacted with over 160 countries. Arrieta led the creation and implementation of the largest public health surveillance capability in the United States during the pandemic and a nationally supervised machine learning implementation to accurately distribute testing supplies and predict pandemic "hot spots" across the country. He successfully defended the HHS network against multiple large-scale nation-state-driven cyberattacks. He led the first three implementations of blockchain technology in the public sector in the United States, one of which was focused on reducing costs and speeding up procurement lifecycle.

Arrieta was a cabinet-level agency executive in the following positions: deputy assistant secretary for acquisition and grants, chief information officer, chief data officer, small business executive chief acquisition executive and senior procurement executive. Arrieta managed the largest contracting vehicle in the United States. He created and taught the first blockchain course (blockchain and cryptos) at Johns Hopkins University as well as entrepreneurial finance.

He founded small incubator called imagineer when he left government. Imagineer is an IT solutions company that currently is focused on developing foundational tools to enable metaverse solutions for sports and entertainment, mental health, hotel and lodging, and sustainable energy market verticals. He has created a secure root of trust, anti-jamming, anti-spoofing, ant hacking, distributed remote monitoring capability for human and machine endpoints. He is currently the Chief Strategy Officer for a publicly traded sustainable energy, health care, and technology company, Dalrada Financial Corporation, and he leads the strategy and commercialization efforts for their commercial heat pump, digital twin, carbon credit platform.

Abstract: Securing Machine Endpoints in a Post-quantum Operating Environment

How to effectively create security around different program logic controllers that exist on machine endpoints is a challenge. The presentation will outline a low-cost effect development, security, and operations approach to creating post-quantum tunnels and security by establishing identities among endpoints at a granular level. The approach will ensure the consistent ability to upgrade inputs into security architecture while delivering at low cost by filling security gaps in the existing architecture.

Reimagining Regulatory Data Submissions through FHIR

Jose Galvez, MD

Deputy Director, Office of Strategic Programs
FDA, Center for Drug Evaluation and Research

Jose Galvez, MD, serves as the Deputy Director for the Office of Strategic Programs (OSP) within FDA's Center for Drug Evaluation and Research (CDER). Prior to joining OSP, Dr. Galvez spent 10 years with the National Institutes of Health, directing the Biomedical Translational Research Informatics Systems at the NIH Clinical Center, as well as directing the Clinical and Translational Informatics program at the Center for Biomedical Informatics and Information Technology at the NIH National Cancer Institute.

Dr. Galvez received his MD at the University of California, Davis, in 1993, where he also did a residency in Pathology and Informatics fellowship. From 2000-2010, Dr. Galvez was an Assistant Professor of Pathology and Director of Bioinformatics at the University of California, Davis, School of Medicine, in the Department of Anatomic and Clinical Pathology. He received his BS in Biochemistry from the University of California Davis in 1997.

Abstract: Reimagining Regulatory Data Submissions through FHIR

The preparation of regulatory submission packages for regulatory agencies is a multi-layered process governed by differing agencies, multiple guidances, complex legal considerations, and not least the coercion of datasets into multiple standards for submission to HAs. While the former is outside of our scope, we will focus on the opportunities for modernization and simplification of the latter.

The current process for the preparation and submission of regulatory data has largely been unchanged for decades. Originally, packages were prepared as correspondences and manuscripts with large amounts of data transcribed onto paper and delivered by the truckload. Regulators were then taxed with the daunting task of combing through the reams of data, validating statistical assertions, and hoping nothing was missed. In today's digital environment, where data is largely produced, stored, and analyzed with the aid of computers, we still ask sponsors to create the same artifacts but have replaced paper with various digital representations. While some data comes nicely packaged in XML or similar formats with known structures and, relatively speaking, is easily transformed from source data system, much data still comes embedded in PDF and DOC formats, which must be "parsed" and interpreted. Modern data representation and transmission standards afford us the opportunity to explore more efficient modes of data transmission. In this talk, we will focus on Fast Healthcare Interoperability Resources as one such technology and its implications to industry and HAs.

Leveraging Large Datasets for the Development and Evaluation of New AI-enabled Medical Imaging Devices

Frank Samuelson, PhD

Physicist
FDA, Center for Devices and Radiological Health

Frank Samuelson, PhD, is a physicist at FDA. His research includes methods of evaluating computational intelligence algorithms found in diagnostic medical imaging devices, including statistical methods and study designs. He studies signal detection in medical images with human observers, and he reviews studies for devices and algorithms for FDA. Prior to FDA, he worked in the area of TeV astrophysics at Los Alamos National Laboratory.

Abstract: Leveraging Large Datasets for the Development and Evaluation of New AI-enabled Medical Imaging Devices

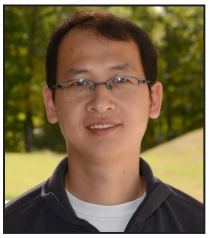
Deep-learning artificial intelligence systems for medical imaging are incredibly complex; some have millions of parameters. These systems function on images, each of which may be many gigabytes in size. To be reliable and generalizable to their intended populations, such systems require training and optimization on very large samples of patient images using very fast computing hardware. Over the last decade several organizations, like the Medical Imaging and Data Resource Center, have amassed large public and private repositories of electronic health records and medical image data. These data have accelerated the development of AI systems that diagnose patients and process medical images. Hundreds of such devices have been submitted to FDA in recent years. Fortunately, these large databases have also facilitated more extensive and rigorous testing of AI systems than was possible just a few years ago. This talk will review and highlight how manufacturers have leveraged these big data resources to develop new artificial-intelligence algorithms and evaluate their safety and effectiveness in submissions to FDA.

Using Genomic Data and Machine Learning to Study Antimicrobial Resistance in Foodborne Pathogens

Amy Merrill, MS
Mathematical Statistician
FDA, Center for Veterinary Medicine

Amy Merrill, MS, joined FDA's Center for Veterinary Medicine (CVM) as a mathematical statistician in 2020. Her primary responsibilities at CVM include study design, data management, data analysis, and data visualizations for the National Antimicrobial Resistance Monitoring System. Her work has focused on the use of whole genome sequencing data to predict antimicrobial resistance and the incorporation of that data in internal and external data tools and visuals. She also collaborates with principal investigators within CVM to assist with statistical analysis and data visualizations for various research projects.

Using Genomic Data and Machine Learning to Study Antimicrobial Resistance in Foodborne Pathogens



Chih-Hao Hsu, PhD
Computer Scientist
FDA, Center for Veterinary Medicine

Chih-Hao Hsu, PhD, holds doctorate in computer science and engineering from Pennsylvania State University in 2009. After graduation, Dr. Hsu worked as a Visiting Fellow at the National Center for Biotechnology Information (NCBI) and as a Research Fellow at the National Cancer Institute. Dr. Hsu joined FDA in 2015 and has provided his bioinformatics expertise in support of the study of antimicrobial resistance for the National Antimicrobial Resistance Monitoring System project.

Dr. Hsu's duties include providing bioinformatics expertise in support of next-generation sequencing and metagenomics data analyses; initiating and performing studies in accordance with Center priorities in collaboration with microbiologists and other scientists within the Center for Veterinary Medicine; working with principal investigators to understand their bioinformatics analysis needs and turning ideas into practical design; and developing new analysis methods, which are applied to problems whose analyses are not supported by usual data analysis methods.

Abstract: Using Genomic Data and Machine Learning to Study Antimicrobial Resistance in Foodborne Pathogens

Foodborne enteric bacterial pathogens, which cause disease and illnesses in humans and animals, are now routinely surveilled using whole genome sequencing (WGS). High-resolution genomic data make it possible to link illnesses to specific sources of contamination, and to make predictions about bacterial phenotypes, like virulence and resistance, to antimicrobials. Scientists in the National Antimicrobial Resistance Monitoring System (NARMS) at FDA's Center for Veterinary Medicine use genomic data and artificial intelligence/machine learning to study antimicrobial resistance (AMR) in Salmonella, E. coli, Campylobacter, and Enterococcus, isolated from retail meats, humans, and food producing animals. There is a high correlation between resistance genotypes and phenotypes, allowing for NARMS scientists to use WGS data to predict phenotypic resistance and report on findings as soon as the WGS is completed, without waiting for additional susceptibility testing. NARMS scientists have implemented the Boost Machine Learning Model to improve upon categorical resistance vs. susceptible predictions by predicting antimicrobial Minimum Inhibitory Concentrations from WGS data. The genomic and artificial intelligence/machine-learning work within NARMS allow for rapid, field-based monitoring of emerging resistance genes and mutations, enhanced accuracy in the prediction of AMR, and an understanding of AMR at a deeper level.

Machine Learning and Case Identification in Claims Data

Ravi Goud, MD, MPH

Medical Officer, Office of Vaccines Research and Review
FDA, Center for Biologics Evaluation and Research

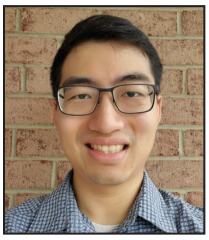
Previously, while in the Office of Biostatistics and Epidemiology, he participated in a variety of pharmacovigilance and informatics activities. This included assisting with the COVID-19 vaccine authorizations and leading studies using claims data. Prior to joining FDA, he led projects for the United States Agency for International Development's MEASURE Evaluation and its Maternal and Child Health Integrated Program, where he focused on malaria, HIV, verbal autopsy, and other infectious diseases. Dr. Goud was also a Peace Corps Volunteer in West Africa.

Abstract: Machine Learning and Case Identification in Claims Data

The accurate detection of outcomes of interest in health-care databases can help harness the potential of big data in health care or public health by enabling the use of available data for surveillance or research purposes. Unfortunately, claims data in health-care databases are meant for administrative purposes, not for research purposes, so the detection of outcomes can be difficult. This is especially true for conditions that can present and be coded in a diverse manner. Machine learning offers a potential solution that permits researchers to take advantage of patterns observed in more dimensions than a human can normally consider.

This presentation will cover the experience of using machine learning to help improve the identification of anaphylaxis, a severe life-threatening allergic reaction, in claims data. Unsupervised and supervised methods were utilized, along with data of varying data quality, as chart-confirmed ground-truth data is frequently rare and arduous to obtain from health-care databases. Based on our experience, we propose a general approach for how machine learning could be used to improve case identification and/or expedite the construction of human expert-driven case identification algorithms.

Using Machine Learning to Predict Non-compliance in the Global Food Supply: Improving Risk-informed Resource Allocation and Public Health Protection



Jeffrey Chou, MSPH
Biologist
FDA, Center for Food Safety and Nutrition

Jeffrey Chou, MSPH, joined FDA's Center for Food Safety (CFSAN) in 2019 as an Oak Ridge Institute for Science and Education (ORISE) Data Science Fellow shortly after completing a master's in biostatistics from Emory University and a bachelor's in microbiology from the University of Georgia. As an ORISE fellow, he built Tableau dashboards for visualizing food safety surveillance sampling activities and developed machine learning (ML) models in Python to predict high-risk food commodities and supply chains for sampling prioritization. In 2021, he accepted a full-time position in the same office, where he continues work on the same ML models as well as extending the framework to other regulatory compliance activities, like predicting high-risk food facilities for inspection prioritization.

Abstract: Using machine learning to predict non-compliance in the global food supply: Improving risk-informed resource allocation and public health protection

More than 90% of seafood sold to US consumers is imported from abroad. While the overall supply chain is safe, potential health hazards from seafood include pathogenic bacteria such as Salmonella and toxic compounds from decomposition such as histamines. Thus, machine learning (ML) was chosen as a tool to better predict and increase rates of violative findings in regulatory sampling of imported seafood as part of a pilot study under FDA's New Era of Smarter Food Safety Blueprint.

We trained a ML model using a boosting algorithm (decision tree-based) called LightGBM using 10 years of previous historical sampling data merged with demographic and compliance data of associated source facilities. The model was then used to score active supply chains and products for the probability of violative microbiological and decomposition findings. A 2x2 factorial design was also implemented to understand not only the main effect of the ML predictions, but also the effect of another existing rules-based sampling targeting model running in FDA's systems called PREDICT (Predictive Risk-based Evaluation for Dynamic Import Compliance Targeting).

While the pilot is still ongoing, interim analysis shows that there is a significantly higher violative rate in the samples of products predicted by the model for such hazards vs. those that were not predicted as violative, even when controlling for the effect of PREDICT. This demonstrates the potential and need for expanding the use of ML to other commodities in sampling and other compliance work, like facility inspections, to ultimately maximize public health benefit with limited regulatory resources.

Guest Panelists

Steve Condrey, MPS

Program Analyst, Division of Quality Management Systems
FDA, Office of Regulatory Affairs

Steve Condrey, MPS, is a program analyst in the Division of Quality Management Systems (DQMS), Office of Regulatory Affairs. Condrey has been with FDA since 1994, starting as a Consumer Safety Technician in the Los Angeles District. Condrey was an Import Operations Consumer Safety Officer (CSO) from 2002-2012 before becoming a Quality System Manager. He has worked with programmatic data since 1996. In 2019, he joined the staff of DQMS, where he worked with the Document Control, Audit, and QMS Training teams. Condrey has worked with R, Python, SAS, and SPSS since 2017. Condrey is a certified Six Sigma Black Belt, certified ISO 9001 Lead Auditor, and American Statistical Association (ASA) Graduate Statistician. In 2022, Condrey served as co-chair of the 10th annual Scientific Computing Days. He is currently co-chair of the FDA Data Science Forum.

Joshua Xu, PhD

Branch Chief, Research-to-Review and Return
FDA, National Center for Toxicological Research

Dr. Joshua Xu received his PhD in Electrical Engineering from Texas A&M University, with research in medical image analysis. He is the Branch Chief for Research-to-Review and Return (R2R) at the Division of Bioinformatics and Biostatistics of FDA's National Center for Toxicological Research (NCTR). He is an expert in next-generation sequencing (NGS) data analysis, image analysis, artificial intelligence, and informatics system development.

His recent focus has been with the FDA-led Sequencing Quality Control Phase 2 (SEQC2) project to evaluate the technical reliabilities and scientific applications of the NGS technologies. He led the SEQC2 Oncopanel Sequencing Working Group to assess the reproducibility and detection sensitivity of oncology panel sequencing, including liquid biopsy tests that analyze circulating tumor DNA in blood to advance precision medicine. The Working Group consists of over 200 participants from academia, government agencies, and industry, including eight companies providing onco-panels and 30 testing laboratories. He is also the Executive Secretary for the international Massive Analysis and Quality Control society.

Guest Panelists *(cont.)*

Yu Mei, DrPH, MPH, MS

Supervisory Regulatory Informational Specialist,
Regulatory Science Informatics
FDA, Center for Tobacco Products

Yu Mei, DrPH, MPH, MS, joins FDA's Center for Tobacco Products (CTP) from a full-stack software developer background/ Previously, he held various technical and management positions, including technical manager, system architect, and team lead. He holds a DrPH, an MPH, an MS in Biology, and a MS in Computer and Information Science. He is currently working on data modernization and is responsible for the Office of Science (OS) enterprise architecture and design. He has also supported CTP's tobacco product review systems, as well as the AI/ML/DS project ASSIST4TOBACCO and Autobots. Currently, he is the team supervisor of the modernization team in the Division of Regulatory Science Informatics in OS/CTP.

Moderator

Hesha J. Duggirala, PhD, MPH

Epidemiologist
FDA, Center for Veterinary Medicine

Hesha J. Duggirala, PhD, MPH is an epidemiologist at the FDA's Center for Veterinary Medicine (CVM). She received her Doctor of Philosophy with a concentration in epidemiology from the Tulane University School of Public Health and Tropical Medicine. Dr. Duggirala joined FDA in 2001 as an epidemiologist in the Office of Surveillance and Biometrics at the Center for Devices and Radiological Health. In 2007, she co-founded, and continues to chair, the FDA Data Science Council (formerly Data Mining Council). This group advises and provides support to data mining programs across the Agency. She was the lead author of the Council's seminal white paper on data mining at the FDA. Dr. Duggirala currently serves as an epidemiologist in CVM's Office of Surveillance and Compliance where she provides epidemiologic support to various groups across CVM as well as developing a framework for the Center's big data analytics programs.

ILMERAC: Sharing Scientific Expertise in the Area of Methodologies for Chemicals in Food with National and International Risk Assessment Agencies across the Globe

Djien Liem, PhD

Team Leader,
Preparedness, Methodology, and Scientific Support Unit
European Food Safety Authority

Djien Liem, PhD, is Head of the Preparedness Team of the Methodology and Scientific Support Unit in the European Food Safety Authority (EFSA). His team carries out activities aimed at the integration of new methods, approaches, and tools in EFSA's risk assessments and supports the work of the Scientific Committee charged with the implementation of guidance documents for EFSA's risk assessments. He started his career in 1986 as Head of the Department of Industrial Contaminants at the National Institute for Public Health and Environment (RIVM), in the Netherlands, where he became involved in dioxin projects of the European Commission and the World Health Organization. He served as a scientific secretary of the European Commission's Scientific Committee on Food from 2000-2002, and he joined EFSA in 2003 as head of the unit supporting EFSA's Scientific Committee. From 2013-2018, he coordinated EFSA's International Scientific Cooperation program, in which he organized the agency's bilateral and multilateral international cooperation with food safety agencies worldwide. Dr. Liem chaired International liaison groups in the area of food contaminants (IFCSLG 2014-2016) and on methods of risk assessment for chemicals in food (International Liaison Group for Methods of Risk Assessment for Chemicals in Food since 2018). Dr. Liem holds a PhD in biology from the Utrecht University and a master's in environmental chemistry and toxicology from the University of Amsterdam.

Abstract: ILMERAC: Sharing Scientific Expertise in the Area of Methodologies for Chemicals in Food with National and International Risk Assessment Agencies across the Globe

Agencies conducting risk assessments informing regulatory measures in the area of food safety are increasingly working together to keep up with evolution in science. The validation, implementation, and acceptance of potential improvements take time. Cooperation among these agencies will therefore help to address these common future challenges in the area of chemical risk assessment. EFSA therefore proposed, at a conference in November 2017, to bring governmental and intergovernmental organizations together to create the International Liaison Group for Methods of Risk Assessment for Chemicals in Food (ILMERAC).

ILMERAC started its activities in February 2018, with more than 20 agencies, with a regulatory risk assessment mandate to share experience, knowledge, and best practices on ongoing and planned activities aimed at implementing new methods for risk assessment of chemicals in food. Various topics, ranging from the assessment of chemical mixtures to the use of alternative methods to animal testing, were discussed,

and participants were given access to all materials considered on a shared repository provided by EFSA. More recently, it was decided to create working groups to have more in-depth discussions on priority topics. A first working group was created to focus on new approach methodologies, and a second working group to address challenges in exposure assessment is currently under consideration.

To date, ILMERAC has brought together more than 80 representatives from 26 organizations to discuss opportunities to integrate new approaches in chemical risk assessment. The achievements of nearly six years of ILMERAC will be summarized.

Progress and Needs for New Alternative Methods in CFSAN's Regulatory Mission

Steven M. Musser, PhD

Deputy Center Director for Scientific Operations
FDA, Center for Food Safety and Applied Nutrition

Stephen M. Musser, PhD, is the Deputy Center Director for Scientific Operations at the Center for Food Safety and Applied Nutrition (CFSAN). In addition to managing the Center's scientific operations, he oversees the Center's activities in cosmetics safety, color certification, pre-market review of food additives, food contact notifications, and foods derived from bioengineered plants. He has directed the Center's research in precedent-setting areas of food and cosmetic safety research, which include food allergen detection, methods for detecting chemical contaminants, dietary supplement analysis, and the use of whole genome sequencing during foodborne illness outbreak investigations. He has authored or co-authored more than 100 articles in the peer-reviewed scientific literature and regularly speaks on CFSAN's research at national and international scientific meetings.

Dr. Musser received his BS in Biology from Millersville University and his PhD in Medicinal Chemistry from the University of Maryland-Baltimore. He then completed a post-doctoral research fellowship at the National Institutes of Health, National Cancer Institute. He started his career at FDA in 1991 as a research chemist and became the Branch Chief of the Instrumentation and Biophysics Branch six years later. Prior to his current appointment, Dr. Musser was the Director of the Office of Regulatory Science at CFSAN.

Abstract: Progress and Needs for New Alternative Methods in CFSAN's Regulatory Mission

CFSAN recognizes that global partnerships are important in advancing the development and acceptance of New Alternative Methods (NAMs). The International Liaison Group on Methods for Risk Assessment of Chemicals in Food (ILMERAC) was created through a partnership with FDA and the European Food Safety Authority, with the goal of facilitating and coordinating research and regulatory efforts on NAMs through an international framework that could provide the best path to harmonized outcomes. Since its creation three years ago, food regulators from other countries have joined including Japan, China, Korea, Singapore, and Canada. ILMERAC's first challenge was to identify cover key data gaps with NAMs, thus minimizing the need for animal studies. Mixtures were identified as a global problem. ILMERAC's second challenge is to provide guidance for using non-guideline studies (i.e., peer-reviewed publications), including harmonized reporting, and to explore the "context of use qualification" approach. ILMERAC's third challenge is to address the levolution of the risk assessment paradigm, facilitating the integration of mechanistic information rather than apical endpoints at the end of a study. Once case studies using these NAMS are available, the global partners will solicit input from relevant stakeholders.

Studies to Assess the Virulence of Enteric Foodborne Pathogens

Steven Foley, PhD

Division Director, Microbiology
FDA, National Center for Toxicological Research

Steven Foley, PhD, is the Director of the Division of Microbiology at the National Center for Toxicological Research (NCTR) and a member of the Senior Biomedical Research and Biomedical Product Assessment Service. Dr. Foley earned his BS in Zoology and his PhD in Cellular and Molecular Biology/Infectious Diseases from North Dakota State University. He completed a postdoctoral fellowship at FDA/CVM, where his research focused on source tracking of Salmonella from food-animal species.

Following his fellowship, Dr. Foley served as an assistant professor at the University of Central Arkansas (UCA). During his time at UCA, Dr. Foley served as a science advisor for the FDA/ORA, where he provided technical advice on research needs and methodologies. He subsequently was an Associate Research Scientist with the National Farm Medicine Center at the Marshfield Clinic, where he led a research program focused on antimicrobial resistance and virulence of foodborne and zoonotic pathogens.

In 2009, Dr. Foley joined NCTR, and his research team has focused on the fields of zoonotic diseases, food safety, and antimicrobial resistance. Dr. Foley is an adjunct professor at the University of Arkansas. In 2018, Dr. Foley was elected to the Arkansas Research Alliance's Academy of Scholars and Fellows.

Abstract: Studies to Assess the Virulence of Enteric Foodborne Pathogens

Salmonella enterica and Escherichia coli are significant causes of foodborne disease worldwide, and many efforts have been made to minimize their impact on human health. The rapid adoption of whole genome sequencing (WGS) for the characterization of these pathogens has provided a wealth valuable data to better understand factors that increase their pathogenicity (virulence). To more fully utilize WGS data, NCTR scientists have developed virulence factor databases and analytical tools to identify putative virulence genes within sequenced strains. These efforts created a user-friendly web-based interface that allows users to upload WGS files, either singly or as a batch, to determine the genes present. Results from these bioinformatic analyses can then be used to try and correlate the WGS findings to detected virulence phenotypes using in vitro, clinical and/or epidemiological approaches.

This presentation provides results of studies that have utilized WGS analyses, coupled with in vitro, culture-based assessment of intestinal epithelial cell invasion and persistence, comparisons of human clinical strains to those from food animals, and strains with different disease phenotypes to assess virulence. In many cases, there is a good connection between the sets of genes predicted through the WGS analyses with the observed virulence phenotypes; however, in other cases, it is not as clear, highlighting the need for continued research and novel approaches to understand virulence.

An Update on NCTR and OCAC's Collaborative Efforts to Support Cosmetics Safety Evaluation

Luísa Camacho, PhD

Deputy Director, Division of Biochemical Toxicology
FDA, National Center for Toxicological Research

Luísa Camacho, PhD, is the Deputy Director of the Division of Biochemical Toxicology at FDA's National Center for Toxicological Research (NCTR). She received a PhD in cell biology from the University of Lisbon, Portugal, and joined NCTR as a postdoctoral fellow in 2007. A primary goal of her research is to elucidate the pharmacokinetics and toxicity of products of interest to FDA, with a particular emphasis in studies that include exposure during the developmental period. A recent research focus has been on studies that aim to evaluate the dermal absorption of cosmetic ingredients using in vivo and in vitro experimental models.

Dr. Camacho has authored over 35 peer-reviewed articles in international journals and five book chapters. She is the Editor in Chief of the Journal of Environmental Science and Health, Part C: Toxicology and Carcinogenesis, and Section Editor for "Pharmacology, Toxicology, Pharmaceutical Sciences" of the journal Data in Brief.

Abstract: An Update on NCTR and OCAC's Collaborative Efforts to Support Cosmetics Safety Evaluation

Cosmetics (products designed to be applied to the human body for cleansing, beautifying, promoting attractiveness, or altering appearance, as defined in the Food, Drug, and Cosmetic Act of 1938) are regulated in the United States by FDA. To help support this regulatory mission, FDA's National Center for Toxicological Research (NCTR) maintains a diverse research portfolio related to cosmetics safety evaluation, developed in close collaboration with FDA's Office of Cosmetics and Colors (OCAC). Ongoing studies will be presented to showcase NCTR's multidisciplinary approach to address regulatory data gaps identified by OCAC and to evaluate novel tools, including human-relevant, non-animal in vitro test systems, which may ultimately be adopted to inform the safety profile of cosmetic ingredients. This FDA cross-center research collaboration addressing New Approach Methods is ever more relevant with the recent enactment of the Modernization of Cosmetics Regulation Act of 2022, which enhances FDA's regulatory oversight of cosmetics and emphasizes that Congress has a sense that animal testing should not be used for safety testing on cosmetic products, with the exception of appropriate allowances.

The US National Antimicrobial Resistance Monitoring System: Helping Ensure the Efficacy of Antibiotics

Patrick McDermott, PhD

Senior Science Advisor for Antimicrobial Resistance
FDA, Center for Veterinary Medicine

Patrick McDermott, PhD, is the Senior Science Advisor for Antimicrobial Resistance in FDA's Center for Veterinary Medicine. He began this position in December 2022 after serving for over 14 years as Director of the National Antimicrobial Resistance Monitoring System, where he was also Director of the Division of Animal and Food Microbiology. Dr. McDermott has worked for over 30 years in the field of antimicrobial resistance (AMR). He has published over 160 peer-reviewed research articles, book chapters and reviews. Dr. McDermott represents FDA on various work groups committed to combating AMR, including the Transatlantic Task Force on AMR and the Quadripartite Technical Group on Integrated AMR Surveillance. He is a fellow of the American Academy of Microbiology, and recipient of FDA's Francis O. Kelsey Award for Excellence and Courage in Protecting the Public Health.

Abstract: The US National Antimicrobial Resistance Monitoring System: Helping Ensure the Efficacy of Antibiotics

The National Antimicrobial Resistance Monitoring System (NARMS) is an interagency program of the US government that tracks antibiotic resistance in foodborne bacteria from foods, animals, and human clinical cases using harmonized methods. NARMS is moving toward a One Health model of resistance monitoring, which incorporates data on environmental surface waters. Research studies comparing whole genome sequencing (WGS) and classical susceptibility testing data for NARMS target bacteria demonstrated a very high concordance between clinical resistance and the presence of known antimicrobial resistance genes. Therefore, WGS has become the primary data set for AMR monitoring in NARMS, with genomes being uploaded into the public domain on a continuous basis in near real time. Data science tools developed at CVM are helping to track resistance at the genetic level and to foster rapid communication and response. Research into metagenomic methods is also being used to catalogue the resistome from various relevant biological samples, including environmental waters. The use of both genomic and metagenomic approaches is providing new insights into the ecology of antibiotic resistance and helping to establish best practices for One Health antibiotic resistance monitoring in the age of genomics.

Moderator

Rajesh Nayak, PhD, MS

Associate Director, Regulatory Compliance and Risk Management
FDA, National Center for Toxicological Research

Raj Nayak, PhD, MS, is the Associate Director of Regulatory Compliance and Risk Management (RCRM) at FDA's National Center for Toxicological Research (NCTR). He earned his MS and PhD in Animal and Veterinary Sciences from West Virginia University. He joined NCTR's Division of Microbiology as an Oak Ridge Institute for Science and Education postdoctoral fellow in 2001. Dr. Nayak's scientific research that supplemented FDA's regulatory decisions to ensure the safety of foods and antibiotics in the "farm-to-the-fork" continuum. His research has focused on epidemiology, surveillance, and microbial source tracking of food-animal infectious pathogens through the food production environment using genotyping methods; threat assessment of emerging pathogens and their genetic characteristics using microarray, sequencing, and bioinformatics platforms; investigating the mechanisms of drug resistance and pathogenesis in bacterial pathogens isolated from food, feed, environment, humans, and veterinary sources; and molecular tools for detecting of bacterial pathogens and their genetic traits.

Dr. Nayak has authored or co-authored more than 70 peer-reviewed scientific publications and book chapters and has given more than 145 presentations at national and international conferences. In 2015, Dr. Nayak joined RCRM as a Senior Health Scientist, where he led NCTR and FDA biosafety programs and regulatory compliance of hazardous biological agent and toxins. In 2018, Dr. Nayak was named Associate Director of RCRM, which is responsible for the following programs: chemical safety, biological safety, radiological safety, controlled substances, quality assurance, occupational health and medical surveillance, laboratory safety, hazardous waste management, industrial hygiene, physical security, records management, and archives. Dr. Nayak serves as a senior advisor and subject matter expert to NCTR and FDA leadership on food safety, antimicrobial resistance, laboratory safety, environmental safety, and occupational safety and health. He serves as an NCTR representative on several FDA committees and working groups.

Speaker Bios and Abstracts

Concurrent Session 6: Medical Countermeasures, Infectious Disease, and Pathogen Reduction Technologies

Introducer and Moderator

Mugimane (Manju) Manjanatha, PhD

Supervisory Research Microbiologist and Deputy Director,
Division of Genetic and Molecular Toxicology
FDA, National Center for Toxicological Research

Manjanatha (Manju) Manjanatha, PhD, is an internationally recognized genetic toxicologist, and his laboratory at National Center for Toxicological Research (NCTR) focuses on research designed to define the pathways from initial DNA damage to mutation leading up to cancer. Dr. Manjanatha recently developed a transgenic hairless albino mouse model for potential application in photocarcinogenicity studies. His research interests also extend to modification of the comet assay for assessment of the genotoxic and epigenetic mode of action of FDA-regulated products as a tool for human risk assessment.

Dr. Manjanatha serves on committees of the Health and Environmental Sciences Institute, Environmental Mutagenesis and Genomics, and Expert Group, OECD Test Guideline development for transgenic rodent model (TG-488) and the comet assay (TG-489) that address the application of transgenic mutational models and DNA damage assays in hazard identification. As Deputy Director of the Division of Genetic and Molecular Toxicology, Dr. Manjanatha oversees the administrative and research responsibilities of around 34 scientists in the division. Dr. Manjanatha has more than 85 publications, has presented at numerous international and national meetings, and serves as editor and editorial board member of many toxicological journals. He has received several FDA major awards over the years.

Investing in the Future of Health Security

Sandeep Patel, PhD

Director, Division of Research, Innovation, and Ventures
HHS, Biomedical Research and Development Authority

Sandeep Patel, PhD, is the Director of the Division of Research, Innovation, and Ventures (DRIVe) at the Biomedical Research and Development Authority (BARDA), within the Department of Health and Human Services (HHS). At DRIVe, he oversees a diverse portfolio of investments, partnerships, and novel financing strategies aimed at advancing potentially transformative technologies and capabilities to improve our ability to prevent, prepare for, and respond to health emergencies such as pandemics. This includes more than 65 technology development partnerships in areas such as microneedle patch-based vaccine delivery, novel and home-based diagnostics, the launch of HHS' first public-private venture capital fund, BARDA Ventures, the BARDA Accelerator Network, and the Blue Knight startup incubator partnership.

Prior to joining BARDA, Dr. Patel was the Open Innovation Manager in the Immediate Office of the Secretary of Health and Human Services, where he founded and led several initiatives aimed at solving long-standing and cross-cutting problems in health. He co-founded and led the $35M+ public-private partnership, KidneyX, which aims to develop breakthrough therapies for kidney disease, notably an artificial kidney to displace dialysis. He also spearheaded the Presidential Advancing American Kidney Health Initiative, which aimed to reform the nation's organ transplant system to improve access to life-saving organs, get more patients off dialysis, and improve prevention of kidney failure. He also led a program that introduced and scaled the use of pull incentives, like incentive prizes, and crowdsourcing to accelerate innovation across the family of HHS agencies. Dr. Patel is a nanotechnologist by training and has built his career around accelerating the pace of innovation in science and technology toward solving problems that advance human health and wellness. He is the recipient of the American Society of Nephrology's President's Medal and the HHS Secretary's Distinguished Service award. He holds a PhD in physical chemistry from the Georgia Institute of Technology and a BA in chemistry from Washington University in St. Louis.

Abstract: Investing in the Future of Health Security

The Biomedical Advanced Research and Development Authority (BARDA) is an operating division under the Administration for Strategic Preparedness and Response of the Office of the Secretary in the Department of Health and Human Services (HHS). BARDA's role is to develop medical countermeasures needed to respond to public health emergencies (PHE) from a variety of threats. BARDA's Division of Research, Innovation, and Ventures (DRIVe) works at different stages of development, taking risks on unusual or undervalued technologies and approaches that lay critical groundwork for PHE response, with impact beyond a particular product. In addition to R&D programs, DRIVe also creates ecosystems to encourage and support development through novel models of partnerships, including accelerator networks and nonprofit venture capital investments.

FDA ARGOS: Where Trusted Sequence Data Meets Quality by Design Approach

Vahan Simonyan, PhD, DSc

Chief Scientist, Embleema
Professor of Bioinformatics and Biostatistics,
George Washington University

Vahan Simonyan, PhD, DSc, is a prolific author of 100 scientific publications in physics, chemistry, quantum mechanics, nanotechnology, biotechnology, population dynamics, and bioinformatics. He is also the recipient of multiple grants and awards for excellence in number of health informatics and biomedical informatics projects. He holds an adjunct professor position at George Washington University, where he teaches and develops curriculums for biomedical big data informatics and biostatistics R&D courses. Dr Simonyan's accomplishments in academic and R&D technology careers have been complemented with the success of technology leadership roles in government, academia, and industry, where he establishes large-scale and complex, science-heavy R&D infrastructures capable of serving worldwide communities for research and regulatory purposes.

Abstract: FDA ARGOS: Where Trusted Sequence Data Meets Quality by Design Approach

Effective diagnosis and understanding of infectious diseases through next-generation sequencing (NGS) requires an extensive and high-quality reference sequence database. To address this critical need, FDA's Medical Countermeasures Initiative has spearheaded project ARGOS. The mission of FDA ARGOS is to create a high-quality, regulatory-grade annotated reference sequence database of biothreat organisms, emerging pathogens, and clinically significant bacterial, viral, fungal, and parasitic genomes; and to provide high provenance, reproducible analytical tools for improving FDA's ability for regulatory evaluation of NGS diagnostic devices using ARGOS data.

The project delivers to the regulatory and scientific community various benefits:

1. A high-quality database for reference-grade pathogen sequences.
2. Quality control (QC) metrics and comprehensive annotations for all sequences.
3. Standardized dictionaries for NGS-based sequence QC metrics.
4. Harmonized tools for sequence QC, annotation, and deposition.

Assessing the Role of T-Cell Responses in SARS-CoV-2 Protection

Marian Major, PhD

Principal Investigator and Laboratory Chief, Laboratory of Hepatitis Viruses, Office of Vaccines Research and Review
FDA, Center for Biologics Evaluation and Research

Marian Major, PhD, is a Principal Investigator and Laboratory Chief of Hepatitis Viruses in the Division of Viral Products in the Office of Vaccines Research and Review. She has more than 24 years of experience in hepatitis vaccine research. Specifically, she focuses on vaccine approaches for the prevention of hepatitis infection. Recently she began a collaboration with mathematicians and social scientists to develop in silico tools to test the impact of intervention strategies, like HCV vaccination, on the incidence of disease in drug user populations. Prior to joining FDA in 1996 as a NIH Fogarty Fellow, Dr. Major was a postdoctoral research fellow at the University of Cambridge. Dr. Major received her PhD in Biology from the University of Warwick, in the United Kingdom.

Abstract: Assessing the Role of T-Cell Responses in SARS-CoV-2 Protection

Correlates of vaccine-induced protection against SARS-CoV-2, and especially the role of T cells, remain incompletely defined. Using mouse models, we are studying vaccination with self-amplifying RNAs (saRNA) encoding the SARS-CoV-2 spike protein or adenovirus vectors expressing the nucleocapsid protein (Ad-N) to further evaluate immunity to COVID-19. Vaccination of K18 transgenic mice with the saRNA expressing spike induced both antibody and T-cell responses that provided protection following viral challenge, in terms of less weight loss, less viral burden, and improved survival. However, these protective outcomes were accompanied by increased inflammation in lungs due to T-cell and B-cell infiltration. Both the protective effects and the inflammatory increases depended on the availability of T cells at the time of challenge. Conversely, vaccination of mice with Ad-N vectors did not result in increased lung inflammation following challenge despite reduced weight loss and lower lung RNA titers. The quality and magnitude of T-cell responses induced during vaccination could be pivotal in the development of vaccine-enhanced respiratory illness for COVID-19 vaccines.

Development of Regulatory Science Tools to Accelerate Development of Medical Devices in Public Health Emergencies

Jenna Osborn, PhD

Scientific Project Manager,
Office of Science and Engineering Laboratories
FDA, Center for Device and Radiological Health

Jenna Osborn, PhD, is a scientific project manager in the Office of Science and Engineering Laboratories (OSEL) at FDA's Center for Device and Radiological Health (CDRH). Dr. Osborn has a PhD in Mechanical and Aerospace Engineering from George Washington University. She received her master's in biomedical engineering from Duke University and bachelor's in physics from Appalachian State University. Dr. Osborn has been working within OSEL since 2019 and has a technical background in biomedical acoustics, computational modelling, and medical imaging.

Abstract: Development of Regulatory Science Tools to accelerate development of medical devices in public health emergencies

The Office of Science and Engineering Laboratories (OSEL) is composed of scientists and engineers who have a broad diversity of expertise from microbiology to artificial intelligence and machine learning. In OSEL, researchers work to develop Regulatory Science Tools (RSTs), which are peer-reviewed resources for companies to use where standards and MDDTs do not yet exist. These tools expand the scope of innovative science-based approaches to help improve the development and assessment of emerging medical technologies. Within OSEL, the Emergency Preparedness Program conducts regulatory science research to help ensure patient access to innovative emergency preparedness devices that are safe and effective. This presentation will include an overview of RSTs and the ongoing work within OSEL's Emergency Preparedness Program.

Development of a Platform Approach to Model Neurotropic Viral Infections and Characterize the Therapeutics That Target Them

Daniela Verthelyi, MD, PhD

Chief, Laboratory of Innate Immunity,
Office of Biotechnology Products
FDA, Center for Drug Evaluation and Research

Daniela Verthelyi, MD, PhD, heads the Laboratory of Innate Immunity and chairs the Center for Excellence in Infectious Diseases and Inflammation in the Office of Pharmaceutical Quality. She directs a lab focused on developing tools to monitor and control innate immune and inflammatory responses. The tools developed by her lab help to elucidate the role of innate immunity in controlling emerging infections such as Zika, Ebola, and SARS-CoV2 and to control and mitigate the impact of potential immunomodulatory impurities in therapeutic products that reduce the risk of unwanted immune responses.

Dr. Verthelyi received her MD from the University of Buenos Aires, in Argentina, and a PhD in Immunology from Virginia Tech. She then joined FDA, where she first completed a fellowship in Retroviral Immunology in the Center for Biologics Evaluation and Research, then she joined the Office of Biotechnology Products in the Center for Drug Evaluation and Research (CDER) as a principal investigator. She has been a driving force in risk evaluation and mitigation pertaining to the immunogenicity of therapeutic proteins, peptides, and oligonucleotides. She has chaired the FDA-NIH Immunology Interest Group, the NIH-FDA Cytokine Interest Group, and served on the Advisory Boards for the NIH Human Immunology Group. She has contributed to multiple FDA Guidances for Industry and MAPPs, authored over 100 scientific papers, holds multiple patents, and received "Excellence in Laboratory Sciences" awards from DA, the Center for Biologics Evaluation and Research, and CDER, among other honors.

Abstract: Development of a Platform Approach to Model Neurotropic Viral Infections and Characterize the Therapeutics That Target Them

Combating emerging new viruses or virus variants would benefit from testing systems that keep up with the evolution of the viruses, while providing consistent measurements of therapeutic activity. Thus, we are developing a platform mouse model that can be used by sponsors to assess the impact of drug products on viral clearance, disease progression, and long-term sequelae of emerging viral infections in vivo using common readouts. Recently, we adapted the platform to develop mouse models for the evolving SARS-CoV-2 and its major variants of concern, and we confirmed the selective therapeutic activity of different monoclonal antibodies. Recognizing that the need to conduct in vivo studies under BSL3 conditions can delay product development and testing, we then generated a BSL2-compatible in vivo system for enveloped viruses using replication competent, GFP tagged, recombinant vesicular stomatitis virus (VSV), where the glycoprotein of the VSV was replaced by the SARS-CoV-2 spike

protein (rVSV-SARS2-S). These models induce symptomatic productive infections that are characterized by neuronal infection and encephalitis, with increased expression of interferon-stimulated genes in the brain, and are uniformly lethal. While the spike protein in different variants are determinants of infectability and virulence, the platform approach may allow for the use the same biomarkers of therapeutic efficacy, reducing the turnaround time for validating each model.

Evaluation of Testicular Organoids as a Model for Zika Virus Infection

Dayton Petibone, PhD

Research Biologist,
Division of Genetic and Molecular Toxicology
FDA, National Center for Toxicological Research

Dayton Petibone, PhD, is a Research Biologist in the Division of Genetic and Molecular Toxicology at FDA's National Center for Toxicological Research (NCTR). Before joining NCTR in 2009, he worked for many productive years in the Department of Biological Sciences at Wayne State University in Detroit, MI. Dr. Petibone received his BS and MS degrees in Biology from Northern Michigan University and his PhD in Applied Bioscience from the University of Arkansas at Little Rock. Dr. Petibone has been a Principal Investigator or Co-investigator on several scientific projects funded through FDA Challenge Grants, including two Medical Countermeasures Initiatives, Perinatal Health Center for Excellence, and the Office of Women's Health grants. Dr. Petibone provides guidance and collaborates with scientists within and outside of FDA on the development and evaluation of microphysiological systems as alternative models for traditional toxicity techniques and as models of Zika virus infection. Dr. Petibone has authored 26 peer-reviewed journal articles and four book chapters.

Abstract: Evaluation of Testicular Organoids As a Model for Zika Virus Infection

Zika virus (ZIKV) can infect testicular cells, replicate, and be sexually transmitted through seminal fluid and sperm, even in the prolonged absence of viremia. ZIKV-infected women who may be or become pregnant might experience pregnancy problems, including fetal loss or congenital Zika syndrome. However, no anti-ZIKV therapies or vaccines are currently approved for use. Here, we describe development and evaluation of non-human primate (NHP) M. mulatta in vitro testicular organoids (NHp-TOs) for use as a model of ZIKV infection. We demonstrated NHP-TO formation and functionality and its susceptibility to ZIKV productive infection for up to 21 days in culture. The system was also suitable to measure testosterone, inhibin B levels, and cytokine secretion, thus demonstrating NHp-TOs to be an appropriate model for studying kinetics of ZIKV infection and pathogenesis in vitro. Such a system will be useful for the evaluation of potential therapies, including anti-viral drugs and antibodies, for treatment of ZIKV infection in the male reproductive system.

Speaker Bios and Abstracts

Concurrent Session 7: Advancing Products Based on Novel Technologies

Update on Personalized Cancer Vaccines

Catherine J. Wu, MD

Professor of Medicine, Harvard Medical School
Chief, Division of Stem Cell Transplantation and Cellular Therapies, Department of Medical Oncology, Dana-Farber Cancer Institute

Catherine J. Wu, MD, is a Professor of Medicine and Chief, Division of Stem Cell Transplantation and Cellular Therapies, at the Dana-Farber Cancer Institute (DFCI). She is a member of the National Academy of Medicine and the Association of American Physicians. She received her MD from Stanford University School of Medicine and completed her clinical training in Internal Medicine and Hematology-Oncology at the Brigham and Women's Hospital and DFCI. She joined the staff at DFCI in 2000. Since then, she has initiated an integrated program of research and clinical activities that focuses on dissecting the basis of effective anti-tumor immunity. Her laboratory has focused on the use of genomics-based approaches to discover immunogenic antigen targets and to understand the molecular basis of therapeutic response and resistance. She has led early phase clinical trials to test personalized tumor vaccines in melanoma and glioblastoma.

Abstract: Update on Personalized Cancer Vaccines

Multiple lines of evidence have convincingly demonstrated tumor neoantigens as an important class of immunogenic tumor antigens, and have motivated the development of personalized cancer neoantigen targeting approaches. Neoantigens arise from amino acid changes encoded by somatic mutations in the tumor cell and have the potential to bind to and be presented by personal human leukocyte antigens molecules. As a field, we have now successfully moved beyond the first wave proof-of-concept studies that have demonstrated the safety, feasibility and high immunogenicity of these personalized vaccines. An imperative now is to address the challenges of discovering and optimizing the selection of antigens to target the delivery approach, and extending this promising approach to a broader array of cancer settings.

Use of NGS Technologies in B-cell Receptor-based Immunome Profiling and MRD Biomarker Discovery

Wenming Xiao, PhD

Lead Bioinformatics Scientist,
Office of Oncologic Diseases
FDA, Center of Drug Evaluation and Research

Wenming Xiao, PhD, has advanced training in biology and computer science. He's published numerous papers in peer-reviewed journals such as Nature, Proceedings of the National Academy of Sciences of the United States of America, and the New England Journal of Medicine, and he received the NIH Director Award in 2010 in recognition of his contributions to cancer biomarkers discovery. Dr Xiao was a principal investigator in FDA and led an international working group to establish reference materials, data sets, analysis pipelines, and quality metrics for cancer mutation detection with next-generation sequencing (NGS) technology, resulting in six manuscripts published in Nature Biotechnology and Genome Biology. In addition, Dr. Xiao was a lead reviewer for NGS-related diagnosis products/applications (510K, IDE, De Novo, or PMA), including Onco-Panel, Whole-Exome Panel, NIPT, Gene Expression Signature, and analytical software (bioinformatics pipelines, knowledge databases). He also provides recommendation on regulatory decisions regarding the safety and effectiveness of medical devices for in vitro diagnostics. Currently, Dr. Xiao is a lead bioinformatics scientist at the Office of Oncologic Diseases, Office of New Drugs, Center for Drug Evaluation and Research.

Abstract: Use of NGS Technologies in B-cell Receptor-based Immunome Profiling and MRD Biomarker Discovery

With the rapid development and adaptation of next-generation sequencing (NGS) technologies, we have the unprecedented opportunity to interrogate many fundamental and transformative questions surrounding the adaptive immune system and human disease. The convergence of high-throughput sequencing technologies, novel analysis methods, and advancements in immunotherapy and drug development has set the stage for standardizing the quantitative study of human immune cell receptor repertoire composition and diversity. The overarching study objectives of this research proposal are to elucidate current limitations, address fundamental technical challenges, provide reference samples and data sets, and establish best practices for reconstructing B-cell receptor repertoires from NGS data. Specifically, with sequencing of contrived samples using short and long-read sequencing technologies, we will critically evaluate and compare sequencing platform, BCR gene mapping/alignment, clonotype classification, diversity, and convergence method and tool to provide best-practice standards and a state-of-the-art analysis framework for B-cell profiling and MRD discovery.

Host-microbiome Crosstalk: Disruption of Gastrointestinal Barrier As Toxicity Assessment Tool

Sangeeta Khare, PhD

Research Microbiologist
FDA, National Center for Toxicological Research

Sangeeta Khare, PhD, is a Principal Investigator at FDA's National Center for Toxicological Research (NCTR) and leads an active team with research emphasis on xenobiotic-host-microbiome interaction. Dr. Khare received her PhD in Infectious Diseases from the All-India Institute of Medical Sciences, in India. She studied gastrointestinal pathogen-host interaction at the University of Saskatchewan, in Canada, and Texas A&M University. Dr. Khare is an adjunct-faculty at Texas A&M.

Dr. Khare has received numerous awards and honors:

- The FDA Group Recognition Award (2022)
- Invited by The European Food Safety Authority as panel member and speaker to the ONE–Health, Environment, Society Conference (2022)
- The NCTR/FDA Special Act Award for outstanding contributions that impact the NTP/NIEHS/NCTR research-initiatives (2019)
- The Indo-US Professorship from the American Society for Microbiology and the Indo-US Science and Technology Forum (2019)

Dr. Khare represents NCTR and FDA in scientific working groups and is Co-Chair of Microbiome Working Group. She is a reviewer/editor for several journals and has served as a grant-reviewer for BARDA, FDA, USDA, NIEHS, and several other international grant organizations.

Dr. Khare's ongoing research is focused on the risk-assessment of xenobiotics on the gastrointestinal tract using animal (gestational and developmental period), and non-animal models employing advanced technologies, like NGS, omics, and systems biology approaches.

Abstract: Host-microbiome Crosstalk: Disruption of Gastrointestinal Barrier as Toxicity Assessment Tool

The human body is exposed to several xenobiotics on a daily basis, including food additives, pesticides, herbicides, drugs, and several other environmental and food contaminants. Exposures to xenobiotics may impact the gastrointestinal barrier and lead to disruptions in the abundance and function of microbiome, antimicrobial resistance, gut mucosa-associated responses, or longer-term disease states. The aim of the research group is to define criteria and build a decision tree for the toxicological assessment at the gastrointestinal tract. The presentation will discuss ongoing approaches, challenges, and opportunities to establish science-based minimum standards for conducting hazard analyses of such products using animal and non-animal models. The outcome of this research will lead to knowledge-based evaluation of xenobiotics using innovative emerging technologies to modernize toxicology.

Regulatory Perspectives on Advancing Regenerative Medicine Products and Emerging Technologies

Carolyn Yong, PhD

Associate Director, Policy and Chief, Policy and Special Projects Staff, Office of Therapeutic Products
FDA, Center for Biologics Evaluation and Research

Carolyn Yong, PhD, leads policy development at the Office-level and develops, advances, and represents Center and Agency level policy positions. Her duties include management of FDA guidance document and regulation development for the Office of Therapeutic Products (OTP) and liaising with other FDA Centers and external stakeholders, particularly in the advancing fields of biomanufacturing and regenerative medicine. She received a PhD in Bioengineering and Biotechnology from the École Polytechnique Fédérale de Lausanne, in Switzerland.

Dr. Yong began her career at FDA as a Regenerative Medicine Commissioner's Fellow and later served as a lead scientific reviewer in the Center for Devices and Radiological Health. Prior to her current role, Dr. Yong served as Device and Combination Products Team Leader in the Division of Cellular and Gene Therapies in OTP, where she conducted scientific regulatory review while providing oversight of programs related to regenerative medicine applications and combination products. She is currently engaged in both FDA and standards organization activities related to tissue engineering and regenerative medicine products.

Abstract: Regulatory Perspectives on Advancing Regenerative Medicine Products and Emerging Technologies

Regenerative medicine is an interdisciplinary field, which aims to restore, replace, or regenerate diseased or damaged cells, tissues, or organs using biological or cell-based technologies. This continuously growing area of biomedical research encompasses cell biology, tissue engineering, drug delivery, and advanced manufacturing, among others. The field of regenerative medicine has made remarkable progress from bench to bedside, bringing reduction in disease burden to patients with limited to no therapeutic options. FDA has oversight of a diverse array of Regenerative Medicine Therapies (RMTs) intended to treat or cure diseases or medical conditions and many of which incorporate or utilize novel technologies. The scientific novelty of RMTs present unique challenges for meeting regulatory requirements. Further, advanced technologies implemented in the development of RMTs can have a significant impact on product development, the manufacturing process, and control strategies, and may also have regulatory implications. FDA plays a critical role in translating innovations into novel, safe, and effective medical products that improve public health.

Dermal Drug Delivery via Dissolvable Microneedles: Formulation Variables Affecting CQAs

Nahid S. Kamal, PhD, MS

Pharmacologist, Office of Testing and Research,
Office of Pharmaceutical Quality
FDA, Center for Drug Evaluation and Research

Nahid S. Kamal, PhD, MS, is a Pharmacologist and CMC reviewer in the Office of Testing and Research under the Office of Pharmaceutical Quality of FDA's Center for Drug Evaluation and Research (CDER). She received her BS and MS from the School of Pharmacy, in Bangladesh, and her PhD in Pharmaceutics from Long Island University. Her research interests include topical and transdermal drug delivery systems, implants, and women's health products, including intra vaginal drug delivery systems. Dr. Kamal has made significant contributions to FDA's initiative related to complex drug products and drug device combinations, under the Generic Drug User Fee Act regulatory science research program. Dr. Kamal has published her work in various peer-reviewed journals and has been awarded many FDA awards.

Abstract: Dermal Drug Delivery via Dissolvable Microneedles: Formulation Variables Affecting CQAs

Dissolving microneedle (DMN) arrays are a micron-sized needle shape dermal drug delivery system that bypasses the stratum corneum following insertion into the skin to deliver drug. Developing DMNs that have desirable critical quality attributes (CQAs), especially optimal mechanical properties to ensure skin insertion and optimal drug release, remains a challenge. To this end, it is important to identify formulation and/or process variables that may impact these CQAs for successful development of DMN arrays and subsequent progression from the bench to the bedside. Our presentation will highlight critical formulation variables (polymer to drug ratio) which may affect the topographical characteristics, drug distribution in the microneedles, mechanical properties (fracture force and skin-piercing ability of the microneedles) and the drug release characteristics of DMN arrays. Our presentation will elucidate the microneedle technology, scientific criticality of its formulation and manufacturability, and the quality aspects that may impact the product performance. The audience will learn how artificial intelligence (AI) segmentation may be employed to assess the topographical characteristics and drug distribution in a DMN array. Additionally, this presentation will provide insight into a novel discriminatory drug release testing method for DMNs. Overall, the presentation will oversee the challenges and successes associated with various characterization approaches for assessing the quality and performance of DMNs.

Assessment of Trabecular Bone Stiffness Using Radiomics and Deep-learning Features

Qian Cao, PhD

Visiting Scientist, Division of Imaging, Diagnostics, & Software Reliability, Office of Science and Engineering Laboratories
FDA, Center for Devices and Radiological Health

Qian Cao, PhD, holds a doctorate in biomedical engineering from Johns Hopkins University. His expertise is in modeling and evaluation of imaging systems, quantitative computed tomography, and image analysis. He is currently a Visiting Scientist in the Division of Imaging, Diagnostics, and Software Reliability, Office of Science and Engineering Laboratories, Center for Devices and Radiological Health, where he provides consultation on the safety and effectiveness of artificial intelligence/machine learning-based medical devices. His current research involves developing radiomics and AI/ML-based tools to improve musculoskeletal imaging and assessment of biomechanics.

Abstract: Assessment of Trabecular Bone Stiffness Using Radiomics and Deep-learning Features

Evaluation of bone fracture risk is important for the diagnosis and treatment of osteoporosis. Bone stiffness is one major factor in determining bone strength and fracture risk. With recent improvements in the spatial resolution of computed tomography (CT) imaging systems, it is possible to visualize bone microstructure and extract texture features. These texture features can be used to construct artificial intelligence/machine learning (AI/ML) models to predict stiffness.

In this work, we developed models utilizing deep learning features, radiomics features, and gradient structure tensors to estimate trabecular bone stiffness in high-resolution CT. We applied these texture-based models to a dataset of trabecular bone region-of-interests (ROIs) extracted from lumbar vertebrae micro-CT images. For each ROI, we used its simulated appearance in high-resolution CT to predict finite element analysis-derived stiffness. We show that texture features can be used to improve the assessment of stiffness compared to using bone mineral density alone. These features may be useful as part of a novel imaging-based biomarkers for osteoporosis therapy studies, potentially streamlining clinical trial designs.

Speaker Bios and Abstracts

Concurrent Session 8: Substance Use, Misuse, and Addiction

Introducer

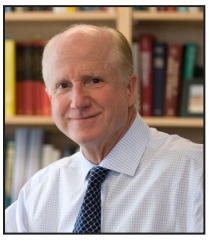
Marta Sokolowska, PhD (Moderator)

Associate Director for Controlled Substances
FDA, Center for Drug Evaluation and Research

Marta Sokolowska, PhD, joined FDA in 2018 as Associate Director for Controlled Substances at FDA's Center for Drug Evaluation and Research. She provides strategic leadership in development and implementation of policies related to controlled substances, including advising on all matters related to domestic and international drug scheduling.

Dr. Sokolowska is a recognized expert in drug abuse potential assessment and scheduling strategies. Throughout her career, she has focused on facilitating initiatives to improve public health by advancing the science of assessing abuse liability. Her past leadership roles include serving as Vice President of Medical and External Affairs at Depomed, Inc. and Head of Medical Affairs at the Center for Abuse Prevention and Evaluation at Grunenthal. Dr. Sokolowska earned her doctoral degree in psychology from McMaster University, in Canada.

Abuse Liability Testing with Humans: A Review of Standard Methods and Recent Innovations Using Cigarettes Varying in Nicotine Content As an Exemplar



Stephen T. Higgins, PhD

Virginia H. Donaldson Professor of Translational Science, Departments of Psychiatry & Psychological Science, Univ. of Vermont
Director, Vermont Center on Behavior and Health

Stephen T. Higgins, PhD, is a Principal Investigator on multiple NIH grants on the general topic of behavior and health, including an NIGMS Center for Biomedical Research Excellence award, a National Institute on Drug Abuse (NIDA)/FDA Tobacco Centers of Regulatory Science award, and a NIDA institutional training award. He has held many national scientific leadership positions, including terms as President of the College on Problems of Drug Dependence and the American Psychological Association's Division on Psychopharmacology and Substance Abuse. He has received numerous national awards for research excellence including a prestigious NIH MERIT award (2001-07) and, more recently, the Association for the Advancement of Behavior Analysis 2022 Translational Science Award and the College on Problems of Drug Dependence 2022 Nathan B. Eddy Memorial Award (a career achievement award).

Abstract: Abuse Liability Testing with Humans: A Review of Standard Methods and Recent Innovations Using Cigarettes Varying in Nicotine Content As an Exemplar

This presentation will provide an overview of methods used in human abuse liability testing using standard and more recent innovations in test methods. Controlled, double-blind, experimental studies conducted to assess whether reducing the nicotine content of cigarettes alters their abuse liability will be reviewed. Testing was conducted with adult volunteers who were current daily cigarette smokers, selected from populations known to be highly vulnerable to chronic smoking, nicotine dependence, and associated adverse health impacts of smoking. Methods to be reviewed include standard subjective-effects questionnaires and drug self-administration procedures as well as more recent and innovative methods such as the hypothetical cigarette purchase task (CPT), wherein experienced users estimate how much product they would consume under varying prices. Results from studies using these standard and more recent methods in the same experiments will be reviewed. Additionally, studies using the more conventional acute testing arrangement, as well as extended exposure testing, will be reviewed.

Field-deployable Analytical Toolkit for Rapid Analysis of FDA-regulated Products at International Ports of Entry

LT Martin M. Kimani, PhD

Senior Regulatory Research Officer
FDA, Office of Regulatory Affairs

LT Martin M. Kimani, PhD, holds a doctorate in bio-inorganic chemistry from Clemson University in 2011. He then completed two years of post-doctoral fellowship with Professor Joseph Kolis in the Clemson University Department of Chemistry. He is also a recipient of the National Research Council post-doctoral fellowship from the National Academies of Science for his second post-doctoral research on heteroepitaxial growth of semiconductors with Dr. Vladimir Tassev and Dr. Matthew Mann at Air Force Research Laboratories at Wright Patterson Air Force Base, Dayton, Ohio, from 2013-2015. He later took the role of a Senior Researcher in thin films growth and radioactive chemistry at the Air Force Research Laboratories, before joining FDA as a chemist in 2017.

Dr. Kimani became a commissioned officer with the United States Public Health Service in 2021 at the height of the COVID-19 pandemic and is currently stationed at FDA's Forensic Chemistry Center as a Senior Regulatory Research Officer. In his current role with FDA, he is involved in forensic investigations of FDA-regulated products due to tampering, counterfeiting, adulteration, and product diversion using lab-based techniques. Additionally, his research has resulted in 37 articles and peer-reviewed publications, and he has developed field-deployable methods able to screen the presence of opioids and other active pharmaceutical ingredients in pharmaceutical products in the field and at US ports of entry.

Abstract: Field-deployable Analytical Toolkit for Rapid Analysis of FDA-regulated Products at International Ports of Entry

In 2021, 128.9 billion units of mail were processed by the United States Postal Service, and many of these items were parcels containing potentially dangerous unknown, unapproved, and misrepresented drug products regulated by FDA. To increase the number of products inspected and help protect consumers, FDA's Forensic Chemistry Center launched a satellite laboratory program outside of the Chicago International Mail Facility (IMF). Two analysts permanently staff this satellite laboratory and analyze samples for the presence of active pharmaceutical ingredients (APIs) onsite, using an analytical toolkit that was extensively evaluated for ruggedness, ease of use, and speed during a pilot study. This toolkit consists of a handheld Raman spectrometer, a portable FT-IR spectrometer, and a portable ambient ionization source, coupled to a mass spectrometer, which has detected over 250 unique APIs in drug products seized during the pilot study and production program.

This program was originally implemented to target opioids, particularly fentanyl and fentanyl analogs, but it has evolved over time to include any type of FDA-regulated products, with an emphasis on complete unknown samples without any type of labeling, which can be challenging even in a traditional brick and mortar lab with an arsenal of well-established analytical techniques. Over the course of 16 months (6/21/2021-10/1/2022), over 1,500 samples were analyzed, and violative samples were referred

to compliance for possible regulatory action, which helped prevent over 350,000 dangerous lot units from reaching the US supply chain. The APIs detected in these samples were either unapproved, controlled substances, and/or fell under the scope of section 801(u) of the Food, Drug and Cosmetic Act, which are drug products that have been deemed by FDA to pose a significant public health concern. Several samples for which the toolkit yielded inconclusive results were sent to a traditional FDA lab for additional/confirmatory analysis.

Here, we delve into the relative merits and limitations of each device, describe the ongoing optimization of the workflow, examine the lessons learned, and discuss plans for future permanent satellite laboratories located at other IMFs.

Blunt and Non-blunt Cannabis Use Associated with Cigarette, E-cigarette, and Cigar Initiation: Findings from the Population Assessment of Tobacco and Health Study

Heather L. Kimmel, PhD

Health Scientist Administrator/Project Officer and Director of the Population Assessment of Tobacco and Health Study, Division of Epidemiology, Services, and Prevention Research, Epidemiology Research Branch; NIH, National Institute on Drug Abuse

At the National Institute on Drug Abuse (NIDA), the program area of Heather L. Kimmel, PhD, includes tobacco regulatory science research and marijuana policy research, as well as the general epidemiology of tobacco and marijuana use, including topics of comorbidity with psychiatric disorders, polysubstance use, and genetic and environmental risk factors for drug use. In addition, Dr. Kimmel is the Director of the Population Assessment of Tobacco and Health (PATH) Study at the National Institutes of Health, which is an ongoing longitudinal cohort study on tobacco use behavior, attitudes and beliefs, and tobacco-related health outcomes, conducted as a collaboration between NIDA and FDA's Center for Tobacco Products.

Prior to joining NIDA, Dr. Kimmel was an American Association for the Advancement of Sciences Science and Technology Policy Fellow at the United States Geological Survey and the Environmental Protection Agency. Dr. Kimmel was an Assistant Professor at the Emory National Primate Research Center as well as in the Department of Pharmacology at the Emory University School of Medicine. There, her research focused on the neuropharmacology and behavior of psychostimulants in animal models as well as the development of medications for psychostimulant use. Dr. Kimmel earned her BS in Biology from Wake Forest University and her PhD in Neuroscience from Emory University.

Abstract: Blunt and Non-blunt Cannabis Use Associated with Cigarette, E-cigarette, and Cigar Initiation: Findings from the Population Assessment of Tobacco and Health Study

Smoking cannabis using a tobacco-derived cigar shell or wrap, called "blunt smoking," exposes its users to non-trivial amounts of nicotine. The extent to which smoking blunts impact the risk of initiating other tobacco products is not well understood. We investigated if past-year blunt smoking is related to th¬e risk of initiating cigarettes, e-cigarettes, and cigars.

Leveraging Systems Modeling to Inform Policies on Opioids

Sara Eggers, PhD

Director, Decision Support and Analysis Staff, Office of Program and Strategic Analysis and Office of Strategic Programs
FDA, Center for Drug Evaluation and Research

Sara Eggers, PhD, directs the Decision Support and Analysis Staff within FDA's Center for Drug Evaluation and Research. This staff leverages decision science principles and tools to help structure, inform, and effectively communicate the Center's drug regulatory decision-making. Through this work, Dr. Eggers has contributed decision science expertise to initiatives regarding drug benefit-risk assessment, patient-focused drug development, product quality assessments, drug safety labeling, risk evaluation and mitigation strategies, and others. In addition, she co-leads an FDA effort utilizing systems modeling to inform policies to address the opioids crisis.

Before joining FDA in 2011, she conducted research and consulting in the areas of decision science, stakeholder engagement, risk management, and risk communication. Dr. Eggers has a PhD in Engineering and Public Policy, with an emphasis on decision science, from Carnegie Mellon University.

Abstract: Leveraging Systems Modeling to Inform Policies on Opioids

Making meaningful gains in the opioid crisis requires interconnected interventions — policies, technologies, services, and communications — all working together. However, assessing the potential public health impact of any one intervention in isolation is extremely challenging in light of incomplete information, complex underlying social phenomena, and the ever-changing opioids landscape. In response to 2017 recommendations from the National Academies of Sciences, Engineering and Medicine, FDA is undertaking efforts to incorporate a systems approach into considerations about the public health impacts of the opioid crisis.

As part of these efforts, FDA has developed, in collaboration with a research team from Harvard/Massachusetts General Health, a national-level system dynamics simulation model of the opioid crisis called SOURCE (Simulation of Opioid Use, Response, Consequences, and Effects). SOURCE is intended to help FDA and other stakeholders identify high-impact interventions concerning opioid misuse prevention, opioid harm reduction, and treatment for opioid use disorder; to assess intended and potential unanticipated consequences of potential policies; and to identify needs for further research. SOURCE has been designed for use within a broader policy analysis service that leverages qualitative and quantitative systems modeling approaches as part of the toolkit of resources informing FDA's policy assessments. The effort has already contributed data-driven insights on underlying trends of the opioid crisis and the potential future effects of broad policy strategies that have informed policy assessments and have helped to advance the use of systems thinking more broadly.

Public Health Harms from Prescription Stimulant Diversion and Nonmedical Use

Rose Radin, PhD, MPH, BS

Team Lead,
Office of Surveillance and Epidemiology, Division of Epidemiology
FDA, Center for Drug Evaluation and Research

Rose Radin, PhD, MPH, BS, is a team lead in the Division of Epidemiology within the Center for Drug Evaluation and Research's (CDER) Office of Surveillance and Epidemiology at FDA. She leads a team of epidemiologists that evaluates post-marketing data on harms associated with the nonmedical use of drugs. Dr. Radin also oversees regulatory research projects. The epidemiology projects that Dr. Radin has conducted or led have informed FDA drug safety communications, safety labeling changes, risk evaluation and mitigation strategy modifications, and FDA Advisory Committee meetings for new drug approvals. Before joining FDA in 2017, Dr. Radin completed a postdoctoral fellowship at the NIH, National Institute of Child Health and Human Development. She received her PhD and MPH in Epidemiology from Boston University and her BS from MIT.

Abstract: Public Health Harms from Prescription Stimulant Diversion and Nonmedical Use

This talk will present the following:

- Trends in the medical use and nonmedical use of prescription stimulants indicated for attention-deficit/hyperactivity disorder.
- Motivations, perceptions, and behaviors related to prescription stimulant nonmedical use, with a focus on young adults.
- Harms from nonmedical use of prescription stimulants and illicit stimulants.
- Concerns about increasing illicit fentanyl and methamphetamine in falsified stimulant products that illicit sellers offer online and may be difficult to distinguish from legitimate prescription products.

Barriers to Prescribing Buprenorphine As a Medication for Opioid Use Disorder: Health-care Providers' Practices, Perspective and Experiences

Matthew Walker, DrPH

Social Scientist, Office of Communications,
Research and Risk Communications
FDA, Center for Drug Evaluation and Research

Matthew Walker, DrPH, is a social scientist in FDA's Center for Drug Evaluation and Research's Office of Communications, Research and Risk Communications (RRC). The RRC conducts research studies aimed at developing evidence to inform CDER's communications, regulatory actions, and policies. Dr. Walker assists with RRC's qualitative and quantitative research studies and social media research on a variety of topics, including opioids, benzodiazepines, and other abusable substances, related to misinformation concerning COVID-19 and other public health emergencies. Prior to joining OCOMM, Dr. Walker worked for FDA's Center for Tobacco Products, Office of Health Communication and Education, where he helped launch national tobacco prevention campaigns and as the Formative Research Team lead.

Abstract: Barriers to Prescribing Buprenorphine As a Medication for Opioid Use Disorder: Health-care Providers' Practices, Perspective and Experiences

Medications such as buprenorphine and methadone can help decrease cravings and relieve withdrawal symptoms for patients with opioid use disorder (OUD), a chronic health condition that can be life-threatening but which is also treatable. To address the significant and growing U.S. opioid addiction and overdose crisis, the federal government in early 2020 eased restrictions on prescribing buprenorphine as a medication to treat OUD. Despite removing the extensive training requirement and need for a special Drug Enforcement Agency waiver to prescribe it for up to 30 patients, the number of clinicians prescribing the medication did not increase.

As part of a qualitative research project led by the Office of Communications within FDA's Center for Drug Evaluation and Research, 16 focus groups (N=143) were conducted among primary care physicians (n=65); physician specialists (n=43); psychiatrists (n=7); physician assistants (n=19), and nurse practitioners (n=9) in late 2021 and early 2022. Qualitative analysis of this feedback was conducted to identify potential barriers to prescribing buprenorphine as MOUD.

Three main barrier-related themes emerged from the data: (1) lack of self-confidence in participants' ability to prescribe buprenorphine, (2) the inconvenience surrounding the practical implications of prescribing the drug and treating patients with OUD, and (3) perceived negative outcomes resulting from prescribing buprenorphine, like the need for intensive follow-up, potential side effects, and a general lack of knowledge about the drug.

These findings provide an increased understanding of barriers to buprenorphine-prescribing practices among US health-care providers that can be used by FDA and others to design educational information and interventions and help inform regulatory actions that can support and advance new and better treatments for people with OUD.

Neonatal Opioid Withdrawal Syndrome: A Scientific and Regulatory Update

An N. Massaro, MD

Supervisory Medical Officer
FDA, Office of the Commissioner (OC)

An N. Massaro, MD, is a pediatrician and neonatologist, and her prior research broadly centers on neonatal neurology and neuroprotection. She did her medical training at Weill Medical College of Cornell University and post-graduate training in Pediatrics and Neonatal-Perinatal Medicine at Children's National Hospital. She joined the faculty at the George Washington University School of Medicine (GWUSOM) after completing training, and she continues part-time as an Adjunct Professor of Pediatrics at GWUSOM and as an attending physician in the neonatal intensive care unit at Children's National. She joined FDA in August of 2020 and currently serves as a Supervisory Medical Officer, overseeing the Neonatology and Rare Pediatric Disease Team in the Office of Pediatric Therapeutics, where she collaborates with centers across FDA to facilitate product development for children with rare diseases and neonates.

Abstract: Neonatal Opioid Withdrawal Syndrome: A Scientific and Regulatory Update

Neonatal opioid withdrawal syndrome, or NOWS (also commonly known as "neonatal abstinence syndrome," or NAS) can occur following in utero transfer of opioid medications or non-prescription opioids to the fetus. Incidence of NOWS is increasing alongside the broader opioid use disorder (OUD) epidemic in the US. Addressing OUD and NOWS are priorities of the Department of Health and Human Services, with ongoing programs including the Advancing Clinical Trials in Neonatal Opioid Withdrawal Syndrome Studies and the HEALthy Brain and Child Development (HBCD) Study specified as part of the National Institutes of Health's Helping to End Addiction Long-term (HEAL®) Initiative.

Recent and ongoing nonclinical and clinical research have helped to increase our understanding of the pathogenesis, clinical course, and long-term neurodevelopmental impact of NOWS. At the same time, knowledge gaps remain and contribute to ongoing challenges with medical product development for treatment of NOWS. Challenges include the reliability of standard methods to assess NOWS severity, clinical variability in approaches to pharmacologic and non-pharmacologic interventions, and selection of clinically relevant endpoints to measure effectiveness of pharmacologic agents and medical devices intended to treat NOWS. This talk will provide an overview of recent and ongoing studies and discuss challenges in developing new therapies aimed at improving outcomes in neonates with NOWS.

Moderator

Arit Harvanko, PhD

Health Scientist
Behavioral and Clinical Pharmacology
FDA, Center for Tobacco Products

Dr. Arit Harvanko's career goal is to improve public health by diminishing the negative impact of tobacco use. At the University of Minnesota he was trained in pre-clinical and clinical settings to conduct research on drug taking behavior and its consequences, and therapies targeted at issues associated with drug dependence. As a graduate student at the University of Kentucky he received training on the behavioral pharmacology of psychoactive drugs and conducted research on the abuse liability of electronic cigarettes. His postdoctoral training at the University of California San Francisco focused on the clinical pharmacology and chemistry of nicotine and tobacco products. Over the past several years Dr. Harvanko has worked in the Behavioral and Clinical Pharmacology Branch in the Center for Tobacco Products. His work there includes tobacco product review and regulation, and conduct of research to inform tobacco regulation.

Virtual Poster Exhibition

The 2023 FDA Science Forum's virtual poster exhibition is scheduled to be available for public viewing on the FDA Science Forum's website from June 13, 2023- July 13, 2023. The audience can directly email their poster-related questions to the poster authors for response.

The virtual poster exhibition will showcase research conducted by the FDA scientists on the Science Forum's eight topic areas:

1. Improving Clinical and Post-market Evaluation
2. Tools to Effectively Use Big Data
3. Empowering Patients and Consumers
4. Product Development and Manufacturing
5. Advancing Products Based on Novel Technologies
6. Medical Countermeasures, Infectious Disease and Pathogen Reduction Technologies
7. Food and Cosmetic Safety
8. Substance Use, Misuse, and Addiction

For more information on the 2023 FDA Virtual Poster Exhibition go to the 2023 FDA Science Forum website

https://www.fda.gov/science-research/about-science-research-fda/fda-science-forum

Acknowledgements

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Session 2: Tools to Effectively Use Big Data

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Session 5: Advancing Products Based on Novel Technologies

Julie Schneider, PhD (OCE)
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Suzanne Fitzpatrick, PhD, DABT (CFSAN)
Donna Mendrick, PhD (NCTR)

Session 6: Medical Countermeasures, Infectious Disease, and Pathogen Reduction Technologies

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Robert Orr, MS (OC)
CAPT Tracy MacGill, PhD (OC)
Todd Myers, PhD (OC)
Dorn Carranza, PhD MBA (CDRH)
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Session 7: Food and Cosmetic Safety

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Suzanne Fitzpatrick, PhD (CFSAN)
Zohra Olumee-Shabon, PhD (CVM)
Priya Kadam, PhD (CFSAN)
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Session 8: Substance Use, Misuse, and Addiction

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