

The 2017 FDA Science Forum



2017 Science Forum

Dates: May 31–June 1, 2017

Location: FDA White Oak Campus & Webcast

Focus: FDA’s use of emerging technologies to advance the knowledge it needs for its regulatory activities and for promoting the development of FDA products that are safe and effective.

Goal: Showcase research at FDA as well as generate collaboration with industry and academia to close FDA knowledge gaps and drive innovation in the science that supports FDA’s mission to protect and advance public health.

Attendance: May 31: 814 (Webcast & on site)

May 31, 2017 – Day 1

Introductory Presentations

Introduction

Bernadette Johnson-Williams, MEd, Senior Advisor for STEM, Office of the Chief Scientist

Video Segment: 0:00 – 04:32

Welcome by FDA Acting Chief Scientist, Luciana Borio, MD

FDA Acting Chief Scientist, Luciana Borio, MD

Video Segment: 04:40 – 13:40

Remarks and Introduction of by FDA Commissioner

FDA Commissioner, Scott Gottlieb, MD

Video Segment: 13:45 - 21:43

Frontiers in Biomedical and Regulatory Science

Eric Lander, PhD, President and Founding Director of the Broad Institute

Video Segment: 21:49 – 13:06

Presentations: May 31, 2017

Morning Concurrent Session 1: Identification and Evaluation of New Biomarkers

Session Chair: Lisa Meier McShane, PhD, Chief, Biostatistics Branch, Biometric Research Program, National Institutes of Health /National Cancer Institute

Food and Drug Administration (FDA)/National Institutes of Health (NIH) Interactions and BEST

Video segment: 0:00-32.54

Lisa M McShane, PhD Chief, Biostatistics Branch, Biometric Research Program, DCTD, NIH/NCI

An ongoing FDA-NIH collaboration to standardize biomarker terminology and study endpoints has led to the development of the Biomarkers, Endpoints, and other Tools (BEST) Resource (<https://www.ncbi.nlm.nih.gov/books/NBK326791/>). The first phase of BEST comprises a glossary that clarifies important definitions and describes some of the hierarchical relationships, connections, and dependencies among the terms. The aim of the harmonized glossary is to strengthen the quality of biomedical research involving biomarkers and make the clinical translation process more efficient.

Biomarker Qualification Program with Update, Case Studies and Challenges

Video Segment: 33:06-52:40

Christopher Leptak, MD, PhD, Associate Director of Biomarker Development Regulatory Science Team, Center for Drug Evaluation and Research

Biomarkers have multiple uses in drug development and clinical trials, including identification of the appropriate patients and prediction of future clinical events of interest. This discussion of CDER's [Biomarker Qualification Program](#) explores how biomarkers can aid in the drug development process and inform regulatory decisions. Topics include: 1) how biomarkers can improve the probability of success or accelerate a drug development program; 2) different classes of biomarkers; 3) a framework to support biomarker development; 4) description of different pathways by which biomarker information can be used to inform regulatory decisions; 5) challenges and solutions to problems in the development and use of an appropriate biomarker during a drug development program.

Biomarker Data in the Population Assessment of Tobacco and Health (PATH) Study

Video Segment: 52:41-1:04:02

Cindy M. Chang, PhD, MPH, Epidemiologist, Office of Science, FDA Center for Tobacco Products on behalf of the PATH Study Team

The [Population Assessment of Tobacco and Health](#) (PATH) Study assesses tobacco use, its determinants, and its impacts among U.S. civilian, non-institutionalized population aged 12 years and older. The goal is to inform research and activities at the [Center for Tobacco Products](#). This study uses biospecimen collection and biomarker testing to characterize tobacco exposures and potential harm from use of different types of tobacco products, including novel products.

Transcript, Proteo, and Metabol-omics as Tools for Translational Biomarker Discovery and Evaluation

Video Segment: 1:04:21-1:14.33

William B. Mattes, PhD, DABT, Director, Division of Systems Biology, National Center for Toxicological Research

The availability of tools that measure a near totality of genes, transcripts, proteins, and metabolites has greatly facilitated the discovery of molecules that serve as biomarkers. For example, following toxicant treatment of mice and rats, miR-122, which appears to be specific for liver injury, can be measured in serum. In addition, studies in mice, rats, and acetaminophen-overdose patients show increases in serum acylcarnitines that precede those of aminotransferases, a possible indication of mitochondrial toxicity. The [BEST](#) (Biomarkers, EndpointS, and other Tools) Resource clarifies terminology and uses of biomarkers and endpoints from basic research to clinical care.

CDRH Perspectives on Imaging Biomarkers Analytical Validation Expectations

Video Segment: 1:14:47-1:23:56

Daniel M. Krainak, PhD, Biomedical Engineer, Center for Devices and Radiological Health

The Center for Devices and Radiological Health is responsible for radiological device pre-market reviews. The center also participates in biomarker qualification review teams for imaging biomarkers through the [Medical Device Development Tools Program](#) (CDRH) and the [Biomarker Qualification Program](#) (CDER). The center takes an evidentiary approach to quantitative imaging devices and imaging biomarkers and its research refines and expands methods for assessing the performance of quantitative imaging biomarkers. This work is key to examining interactions between claims and analytical validation expectations.

Next-Generation Sequencing (NGS): FDA Approval of the 1st NGS Companion Diagnostic

Video Segment: 1:24:15-1:35:19

Hisani Madison, PhD, MPH, Scientific Reviewer, Center for Devices and Radiological Health

A companion diagnostic device is an *in vitro* diagnostic device that provides information that is essential for the safe and effective use of a corresponding therapeutic product. On December 19, 2016 FDA granted simultaneous approval to Rubraca (rucaparib) to treat women with a certain type of ovarian cancer and the FoundationFocus CDX_{BRCA} companion diagnostic indicated to select patients for treatment with Rubraca. The FoundationFocus CDX_{BRCA} test is the first next-generation-sequencing (NGS)-based companion diagnostic approved by the agency. The presentation provides an overview of FDA's review of the FoundationFocus CDX_{BRCA} test and highlights some of the regulatory considerations and emerging complexities that are unique to precision medicine.

Q & A Panel

Video Segment: 1:35:30-1:53:11

Lisa Meier McShane, PhD; Christopher Leptak, MD, PhD; Cindy M. Chang, PhD, MPH; William B. Mattes, PhD, DABT; Daniel M. Krainak, PhD; and Hisani Madison, PhD, MPH

Poster Session 1 [Day 1, AM]: [Identification and Evaluation of New Biomarkers](#) (Pgs. 61 – 80)

Morning Concurrent Session 2: FDA Response to Urgent Public Health Needs

Session Chair: RADM Palmer Orlandi, Jr, PhD, Chief Science Officer and Director of Research, Office of Foods and Veterinary Medicine

FDA's Coordinated Response to Recent Foodborne Outbreaks

Video Segment: 0:00-23:12

CDR Kari Irvin, MS, CORE Response Manager, Center for Food Safety and Applied Nutrition

The FDA [Coordinated Outbreak Response and Evaluation](#) (CORE) Network is a 34-member team that coordinates the flow of information during and after outbreaks involving human food, dietary supplements, and cosmetics. In 2017, FDA CORE coordinated two high profile outbreak investigations: *E. coli* O157:H7 in soy nut butter and *Listeria monocytogenes* in soft cheese. These outbreak responses highlight the importance of establishing an organized and systematic approach to identifying and responding to foodborne emergencies to protect the health and safety of consumers.

Characterization and Analysis of Multidrug Resistant Foodborne Pathogens

Video Segment: 23:21-37:49

Heather Tate, PhD, MS, Epidemiologist, Center for Veterinary Medicine

Scientists from the [National Antimicrobial Resistance Monitoring System](#) (NARMS) collected and sequenced the genomes of ten *Salmonella enterica* serovar Infantis containing *bla*_{CTX-M-65} isolated from chicken, cattle, and human sources. All U.S. isolates were closely related, indicating a high likelihood that strains from humans, chicken, and cattle recently evolved from a common ancestor. This is the first report of the *bla*_{CTX-M-65} gene and the pESI-like megaplasmid from *S. Infantis* in the United States. The finding illustrates the importance of applying a [Global One Health](#), human and animal perspective to combat antimicrobial resistance.

Forensic Analysis of a Mass Poisoning in Mozambique Associated with a Homebrewed Beverage

38:15-53:11

Travis Falconer, PhD, Chemist, Office of Regulatory Affairs

In 2015, the Mozambique Ministry of Health (MOH) and the U.S. Centers for Disease Control and Prevention (CDC) linked the occurrence of a widespread illness in a Mozambique village to the consumption of a homemade, traditional African beer called pombe. At the request of MOH and CDC, the [Forensic Chemistry Center](#) (FCC) of FDA/ORA analyzed the brew and found that it contained potentially fatal levels of the potent toxin bongkreikic acid. The microorganisms that produced the toxin were isolated from corn flour, a starting ingredient. The results suggest a mechanism for bongkreikic acid intoxication, a phenomenon previously thought to be restricted to specific regions of Indonesia and China.

Use of an FDA Real Time Mobile Communication Platform System during Medical Countermeasure Events: RAPID

Video Segment: 53:20-1:11:00

Henry "Skip" Francis, MD, Director for Data Mining and Informatics Evaluation and Research, Center for Drug Evaluation and Research

FDA's Real-Time Application for Portable Interactive Devices (RAPID) System facilitates the real-time collection, analysis, and communication of medical countermeasure (MCM) product information during

chemical, biological, radiological, nuclear (CBRN), and emerging infectious disease events. RAPID provides bi-directional information transmission for drug safety information and provides real-time data analysis system to FDA scientists. It addresses 1) product safety, 2) Risk Evaluation and Mitigation Strategies (REMS), and 3) medication errors. RAPID will also support mobile data collection (e.g., speech-to-text patient and physician narratives) and bidirectional communication between FDA and news media to promote transparency and information-sharing.

Development of Total and Neutralizing Anti-Ebolavirus Antibody Assays for Deployment in West Africa to Evaluate Clinical Trials of MCMs, including Vaccines and Immunotherapies

Video Segment: 1:11:20-1:28:50

Gerardo Kaplan, PhD, Principal Investigator, Office of Blood Research and Review, Center for Biologics Evaluation and Research

Evidence from studies in nonhuman primates suggests that development of high levels of Ebola virus (EBOV) antibodies could be used as a correlate of immunity for some vaccine candidates. However, studies using EBOV to assess total and neutralizing antibodies require Biosafety Level (BSL)-4 conditions that are difficult and time-consuming. Therefore, there is a need for assays appropriate for EBOV BSL-2 conditions to evaluate EBOV total and neutralizing anti-EBOV glycoprotein (GP) antibodies levels. We developed BSL-2 EBOV antibody assays to analyze total antibodies by a virus particle ELISA (VP-ELISA) and neutralizing antibodies by a fluorescence reduction neutralization test (FRNT). We are field testing it with the Italian National Institute of Infectious Diseases to determine if it can be used in resource-limited settings.

Development of Mouse Models to Assess Efficacy and Potency of ZIKA Virus Therapeutics

Video Segment: 1:29:00-1:47:46

Daniela Verthelyi, MD, PhD, Lab Chief, Office of Biotechnology Products, Center for Drug Evaluation and Research

We established and characterized a new model of peripheral Zika virus (ZIKV) infection using immunocompetent neonatal C57BL/6 mice that replicates many features of the human disease and that characterized the clinical progression, virus distribution, immune response, and neuropathology of the disease. The development of our model of ZIKV infection provides insight into the immunopathology of the virus and provides FDA with a platform to facilitate its assessments of therapeutics and vaccines.

Q&A Session

Video Segment: 1:48:00-2:07:00

Poster Session 1 [Day 1, AM] FDA Response to Urgent Public Health Needs (Pgs. 81 – 101)

Afternoon Concurrent Session 3: Microbiome and Human Health

Session Chair: Ryan Ranallo, PhD, Program Officer, National Institutes of Health/National Institute of Allergy and Infectious Diseases

The Human Microbiota in Health and Disease: Overview

Video Segment: 0:00-15:32

Ryan Ranallo, PhD, Program Officer, National Institutes of Health, National Institute of Allergy and Infectious Diseases

The human microbiota contributes to human development in a variety of ways, e.g., by providing key signals to the developing immune system and protecting against microbial pathogens. Recent advances have dramatically enhanced our perspective on how the composition and function of the gut microbiota contribute to diseases, ranging from inflammatory disorders of the gut to cardiovascular illnesses. This review of the human microbiome includes some recent advances in microbiome science.

MetaGenomeTrakr and Food Safety Microbiome Research at Center for Food Safety and Applied Nutrition (CFSAN)

Video Segment: 15:32-31:30

Andrea Ottesen, Ph.D, Research Microbiologist, Center for Food Safety and Applied Nutrition

The metagenomic description of microbiota along the “farm to fork” continuum can identify environments and conditions that may play important roles in introducing pathogens to food. Data from metagenomic research at CFSAN supports the evolution of Good Agricultural Practices (GAPs) and [Food Safety Modernization Act \(FSMA\)](#) regulations. Newly developing microbiome-based approaches to source tracking are improving response time such that these methods, when leveraged correctly, could reduce the number of illnesses associated with any given foodborne outbreak by as much as 75%.

MAIT Cells Alter the Murine Microbiome Reducing Colonization Resistance against *Clostridium difficile*

Video Segment: 31:31-44:39

Paul Carlson, PhD, Senior Staff Fellow, Center for Biologics Evaluation and Research

Clostridium difficile (*Cd*) infection (CDI) typically occurs following antibiotic use, which perturbs the gut microbiota, leaving the host susceptible to *Cd* colonization. Mucosa-associated invariant T cells (MAIT) recognize intermediates of riboflavin biosynthesis presented on MR1, an MHC-I like molecule. To test our hypothesis that MAIT cells play a role in CDI, we treated WT and MR1^{-/-} mice (i.e., mice lacking MAIT cells) with antibiotics, before infecting them with *Cd* spores. We found that MR1^{-/-} were completely resistant to CDI and exhibited significantly different microbiome compositions than WT mice. Our data

suggest that the MR1-/- gut microbiome is resistant to Cd colonization and this resistance is transferrable via fecal matter transplant.

The Effect of Chlortetracycline on Swine Fecal Microbiome and Resistome

Video Segment: 44:45-1:05:22

Daniel A. Tadesse, PhD, Research Microbiologist, Center for Veterinary Medicine

The increasing prevalence of human antibiotic resistance and its link to antibiotic use in animal agriculture is not fully understood. Our study in piglets provides insights into the impact of different concentrations of chlortetracycline (CTC) exposure on swine intestinal microflora as observed by targeted and shotgun metagenomics. The effect of CTC on the swine intestinal microbiota varied by dosage and duration; the changes in relative abundance were more at the genus and species level than at the phylum level. The majority of antibiotic resistance-associated sequences found in control and treated pigs fecal samples belonged to tetracycline resistance. *tet* resistance gene alleles observed varied by dose, and their abundance increased as the duration of CTC exposure increased. The talk highlights the impact of CTC exposure on swine intestinal microflora and resistomes.

Interaction of Silver Nanoparticles beyond Intestinal Bacterial Microbiota: Effects of Intestinal Virome and phages

Video Segment: 1:05:30-1:22:12

Sangeeta Khare, PhD, Research Microbiologist, National Center for Toxicological Research

There has been a significant increase in incorporation of silver and silver nanoparticles (AgNP) into health-supplements, food packages, baby products, and several household items. Our study using both *in vitro* and *in vivo* models showed that small AgNP could lead to perturbations of the gut microbial ecosystem, leading to inactivation of resident gut viruses and phages that play an important role in gut-associated immune responses and in gastrointestinal health. The results of this study support the integration of data from intestinal toxicity (microbial as well as gut-associated immune responses) as an additional endpoint in the risk assessment of the nanoparticles to enhance product safety.

Impact of TNF Antagonist Treatment on the Gut Microbiome: An in Vivo Pilot Study

Video Segment: 1:22:20-1:39:20

Odile Engel, PhD, Researcher, Center for Drug Evaluation and Research

Biologic therapeutics have been used successfully to treat auto-immune diseases; however, they present some unique regulatory challenges. The response to these therapeutics can initially be quite variable among patients, and patients who are initially responsive can develop resistance to them over time. Our study provided evidence that the gut microbiome plays a role in the initial variability and has an impact on the response to treatments.

Q&A Panel

1:39:23-2:05:52

Poster Session 2 [Day 1, PM] [Microbiome and Human Health](#) (Pages 112-121)

Afternoon Concurrent Session 4: Advanced Manufacturing and 3D Printing

Session Chair: Andy Christensen, President, Somaden LLC

[A Historical Perspective of 3D Printing in Clinical Medicine](#)

Video Segment: 00:00 – 17:13

Andy Christensen, President, Somaden LLC

This presentation focuses on the progression of the medical use of [3D printing](#). 3D printing in medicine is usually used to produce complex, patient-matched objects for pre-operative planning, intra-operative reference, and simulation. Its use to create metal implants has recently gained popularity due to its ability to produce complex, porous geometries often used as bone in-growth surfaces.

[Techniques for Performance and Process Evaluation of Advanced Manufacturing](#)

Video Segment: 17:14 – 30:15

LCDR James Coburn, MS, Sr. Research Engineer, Center for Devices and Radiological Health

This talk explores the unique technical aspects and measurement challenges of 3D-printed medical devices. 3D printing is used to create complex lattice geometries for implants and to make patient-matched devices. FDA's Center for Devices and Radiological Health (CDRH) has cleared and approved several types of 3D-printed medical devices through its existing regulatory pathways. The speed of technology's adoption has led to a growing need for best practices for 3D printed medical products. Regulatory science research at CDRH is helping the Agency develop an understanding of the unique technical aspects and challenges inherent in 3D printing and other emerging technologies to facilitate future innovation. Two research snapshots describe how we developed a custom set of surgical cutting guides and ran a mock surgery with orthopedic surgeons of varying skill levels to compare use and outcomes with traditional instruments. The second research project evaluated the effectiveness of cleaning protocols for 3D-printed lattice structures.

Continuous Manufacturing Technologies Celia Cruz, PhD, Division Director, Center for Drug Evaluation and Research

Video Segment: 30:22 – 46:52

Celia Cruz, PhD, Division Director, OPQ, CDER

FDA has committed to continuous manufacturing innovation via programs such as the [Emerging Technology Team](#), regulatory research, and the engagement of FDA experts in professional, regulatory, and academic groups focused on [continuous manufacturing](#) (CM). This talk covers the salient features of previous and emerging proposals for CM, the technical and regulatory challenges, and the opportunities for advancing pharmaceutical manufacturing.

Manufacturing the Seasonal Flu Vaccine

Video Segment: 47:03 – 1:03:46

Zhiping Ye, MD, PhD, Senior Investigator, Center for Biologics Evaluation and Research

There are three types of [seasonal influenza vaccines](#) approved for use in the U.S.: inactivated, live attenuated, and recombinant. This talk describes how they are made and how CBER develops and calibrates potency reagents for these products. Manufacturers and CBER use these reagents to test the vaccines for potency and identity before formulation of the influenza vaccines for U.S. distribution.

Practical Microscale Technologies in the Assessment of Advanced Therapeutic Products in Center for Biologics Evaluation and Research

Video Segment: 1:03:55 – 1:18:18

Kyung Sung, PhD, Principal Investigator, Center for Biologics Evaluation and Research

Multipotent stromal cells (MSCs) are popular sources for manufacturing [Regenerative Medicine Advanced Therapy](#) (RMAT) products due to their ability to undergo lineage-specific differentiation in distinct manufacturing conditions. Successful clinical translation of such cell-based products is often hindered by manufacturing hurdles and the lack of reliable markers that can predict the products' *in vivo* performance. This presentation describes practical micro-scale technologies for identifying cellular markers that can predict *in vivo* performance of products.

Continuous Bio-manufacturing Technologies

Video Segment: 1:18:31 – 1:35:45

LCDR Cyrus Agarabi, PharmD, RPh, MBA, PhD, Regulatory Research Officer, Center for Drug Evaluation and Research

This overview of bioprocessing and regulatory research capabilities in the Office of Biological Products (OPB) focuses on monoclonal antibodies production. OPB uses these capabilities to study continuous bioreactor cell culture production, equipment and [Process Analytical Technology](#) (PAT) tools. The

presentation includes case studies of collaborative laboratory regulatory research being done in these areas to support regulatory decision-making.

Advancing Characterization of 3D-Printed Tissue Engineered Scaffolds

Video Segment: 1:35:57 – 1:50:30

Maureen Dreher, PhD, MS, Research Biomedical Engineer, Center for Devices and Radiological Health

A wide variety of additive manufacturing printer types and process parameters can control the scaffold pore space and its organization at a high resolution. However, this requires significant optimization to achieve the desired quality. In addition, the complex geometries at the micro-scale level in tissue engineered scaffolds make it difficult to measure quality. This presentation discusses the use of non-destructive x-ray based imaging (microCT) to characterize the microstructure of scaffolds and optimization procedures to increase part fidelity for tissue engineered scaffolds manufactured from custom and proprietary materials.

Advanced Manufacturing and 3D Printing Q & A Panel

Video Segment: 1:51:00 – 2:08:16

Poster Session 2 [Day 1, PM] Additive Manufacturing and 3D Printing (Pgs. 102-111)

Presentations: June 1, 2017

Morning Concurrent Session 5: Omics Technologies at the FDA

Session Chair: Minnie Sarwal, MD, FRCP, DCH, PhD, Professor of Surgery, Director Precision Transplant Medicine, University of California, San Francisco, FDA Science Board member

Overview

Video Segment: 0:00 - 23:16

Minnie Sarwal, MD, FRCP, DCH, PhD, Professor of Surgery, Director Precision Transplant Medicine, University of California, San Francisco, FDA Science Board member

New “omic” hypothesis-generating approaches provide the critical data needed for precision medicine. Some of the new technologies and applications of omic approaches will be reviewed. Before omic approaches can be incorporated into patient care, omic-generated data must be validated by biological testing, often on more focused targets in independent samples, must receive endorsement from payers, and needs to be recognized as meeting critical public health needs. This talk will review the recent technologies and general approaches that facilitate precision medicine.

FDA-led community-wide Sequencing Quality Control Consortium 2- (SEQC2)

Video Segment: 23:20 - 37:09

Weida Tong, PhD, Division Director, Bioinformatics and Biostatistics, National Center for Toxicological Research

The use of constantly evolving, high-throughput genomics technologies to assess safety and efficacy of FDA-regulated products raises concerns about their reliability and robustness in supporting FDA's regulatory decision-making. This talk will describe the work of the FDA-led [Microarray/Sequencing Quality Control \(MAQC/SEQC\)](#) consortium in addressing reproducibility, precision, specificity, sensitivity, and interpretation of these technologies. The ultimate goal of the project is to develop standards for using next-generation sequencing data to provide FDA with objective criteria and metrics for assessing the integrity of data used in regulatory settings, and to inform precision medicine.

FDA's GenomeTrakr Program: Advancing Food Safety through Whole-Genome Sequencing of Foodborne Bacteria

Video Segment: 37:20 - 51:48

Errol Strain, PhD, Director, Biostatistics and Bioinformatics Staff, Center for Food Safety and Applied Nutrition

In 2013, the [Center for Food Safety and Applied Nutrition](#) set up a pilot project at the national level using whole genome sequence data (WGS) to track foodborne outbreaks. This pilot, now a mature network, is called [GenomeTrakr](#). In this network, public health agencies collect and publicly share WGS data in real

time. This high-resolution, rapidly growing database is used in outbreak investigations at the state, national, and international level.

MicroRNA Biomarkers of Acute Pancreatic Injury Use

Video Segment: 52:00 - 1:11:20

Rodney Rouse, DVM, MBA, PhD, Acting Associate Director, Division of Applied Regulatory Science, Office of Translational Science, Center for Drug Evaluation and Research

This presentation provides an overview of the animal model investigation by the [Division of Applied Regulatory Science \(DARS\)](#) of microRNAs (miRNAs) enriched in pancreatic tissue as non-invasive, tissue-specific biomarkers of acute pancreatic injury. These miRNAs have significant potential as biomarkers: They rapidly appear in a highly stable form in serum and urine following pancreatic injury and have highly conserved sequence between species. The study demonstrates the usefulness of next generation sequencing in such studies to enhance the profile of these miRNAs as biomarkers of acute pancreatic injury.

FDA-ARGOS Microbial Reference Genomes for Regulatory Use: Zika and Ebola

Video Segment: 1:11:39 - 1:29:13

Heike Sichtig, PhD, Subject Matter Expert, Principal Investigator, Center for Devices and Radiological Health

FDA and collaborators established a publicly available database for reference grade microbial sequences called [FDA-ARGOS](#). The FDA-ARGOS team is collecting and sequencing 2000 microbes that include bio-threat micro-organisms, common clinical pathogens, and closely related species. Manufacturers that develop sequence-based tests to identify infectious agents and/or to detect resistance or virulence markers can use FDA-ARGOS to further their development programs and support the regulatory science review of such tests. This presentation will focus on the FDA-ARGOS sequencing pipeline, including Zika and Ebola reference genomes.

Glycomics Work-Flows for the Characterization of Vaccine Glycoprotein Antigens

Video Segment: 1:29:22 - 1:47:43

John Cipollo, PhD, Principal Investigator, Lab of Bacterial Polysaccharides, Center for Biologics Evaluation and Research

Influenza hemagglutinin glycoprotein is the major antigen in seasonal and pandemic influenza vaccines. As the virus propagates through the human population it tends to gain glycosylation sites as part of its adaptive process. This presentation will discuss how analysis of glycoproteins is used to characterize influenza antigens and how hemagglutinin glycosylation can affect influenza vaccines and the virus's interactions with the host.

Q&A Panel

Video Segment: 1:47:50 - 1:57:29

Poster Session 3 [Day 2, AM] [Omics Technology at FDA](#) (Pgs. 104-154)

Morning Concurrent Session 6: Patient and Consumer Engagement and Communication

Session Chair: Brian J. Zikmund-Fisher, PhD, Associate Professor of Health Behavior and Health Education, University of Michigan

Overview

Video Segment: 0:00 - 4:49

Brian J. Zikmund-Fisher, PhD, Associate Professor of Health Behavior and Health Education, University of Michigan

Use of Flavored Tobacco Products: Findings from the Population Assessment of Tobacco and Health (PATH) Study

Video Segment: 4:50 – 20:21

Bridget Ambrose, PhD, MPH, Branch Chief, Center for Tobacco Products

Reviews of internal tobacco industry documents indicate that some manufacturers historically added flavors to tobacco to attract young consumers. This presentation will describe recent findings about flavored tobacco use from the [Population Assessment of Tobacco and Health \(PATH\)](#) study—a joint collaboration between FDA and NIH, enrolling over 46,000 civilian, non-institutionalized youth and adults via household-based interviews. Findings from this research provide insight into the role that characterizing flavorings may play in promoting the use of non-cigarette tobacco products, particularly among youth and young adults.

Understanding Mothers' Attitudes and Motivations Regarding Menu Labeling: Testing Messaging Concepts and Treatments

Video Segment: 20:30 - 36:41

Kathleen Yu, MPH, Social Scientist, Center for Food Safety and Applied Nutrition

On December 1, 2014, FDA published a final rule requiring restaurants and similar retail food establishments that are part of a chain with 20 or more locations to provide calorie and other nutrition information for standard menu items, including food on display and self-service food. To support the implementation of the rule, FDA will develop educational materials to help consumers interpret and use the information. As a first step in this effort, qualitative data were collected from 16 consumer focus groups to explore and understand how to reach and communicate with consumers on menu labeling. Overall, the

focus groups highlighted the importance of targeted messaging and provided valuable findings of the motivations of middle-income mothers when they are eating out.

Development of Tools to Capture the Patient Perspective with Implantable Minimally Invasive Glaucoma Surgical (MIGS) Devices

Video Segment: 36:50 - 51:37

Michelle Tarver, MD, PhD, Medical Officer, Center for Devices and Radiological Health

Ophthalmologists are increasingly using [minimally invasive glaucoma surgical \(MIGS\) devices](#) to lower pressure in the eye. However, prior evaluation of these devices has not incorporated patient preference information insight on the relative desirability and acceptability of the benefits and risks of these therapies. In addition, patient-reported outcome (PROs) measures, which are often incorporated into clinical trials for MIGS devices to capture ocular symptoms and visual function, may not have undergone a development process sensitive to mild to moderate glaucoma patients undergoing surgery. This discussion summarizes the results of focus group studies that support development of a survey for quantitatively assessing patient preferences. These efforts will help incorporate patients' perspectives into the MIGS device development and evaluation process.

Upper Limb Prostheses Patient Preference Study to Inform Clinical Trial Design and Regulatory Decisions

Video Segment: 51:44 - 1:04:25

Heather Benz, PhD, Medical Device Fellow, Center for Devices and Radiological Health

Current prostheses do not fully meet the needs of individuals with upper limb amputation and congenital limb difference, as demonstrated by prosthesis rejection, non-wear, and reports of pain and challenging activities. Emerging technologies, such as electrical stimulation for the restoration of sensation, implantable neural interfaces for improved prosthetic control, bone-anchored devices, and dexterous "sensorized" robotic limbs, have the potential to provide novel benefits. However, these technologies also pose risks. We conducted qualitative interviews, focus groups, and surveys of individuals with upper limb amputation or congenital limb difference to identify attributes for use in developing patient preference surveys. These surveys are designed to provide researchers with a better understanding of how novel technologies can address patient concerns and inform implementation of new technologies and regulatory decision-making.

Advancing the Science of Patient Input in a Regulatory Setting through Internal Capacity-Building and Research

Video Segment: 1:04:29 - 1:21:07

Million Tegenge, PhD, RPh, Visiting Scientist, Center for Biologics Evaluation and Research

There is currently a demand for more systematic and quantitative approaches to incorporate patient input throughout the medical product lifecycle, including regulatory benefit–risk assessments. The use of patient

preference information (PPI), elicited using established scientific methods, is a promising strategy for accomplishing this. This presentation presents an overview of efforts to advance the science of patient input (SPI) in a regulatory setting, e.g., regulatory projects that aim to incorporate quantitative patient preference data for informing preference-sensitive decisions.

Communicating Risk Information about Drugs: the Effect of Quantitative Information Type on Risk Perceptions and Understanding

Video Segment: 1:21:10 - 1:36:59

Paula Rausch, PhD, RN, Associate Director, Research and Risk Communications, Center for Drug Evaluation and Research

This presentation summarizes results of two experimental surveys that assessed consumer reaction to different types of quantitative information about a drug safety issue regarding respondents' perceived severity of the risk, their personal susceptibility to it and susceptibility of the typical person, and their understanding of the quantitative information. The respondents comprised individuals with either diabetes or constipation who read a paragraph reporting information about a safety issue with a medication used to treat their respective conditions. The main finding suggested that including either quantitative or qualitative information about the frequency of the drug safety issue can lower risk perceptions, which may help reduce potential unintended effects of these types of communications, such as stopping a needed medication. The study also found that overall understanding of quantitative information was low, and that no type of quantitative information improved understanding. Importantly, these experiments also showed that the type of medical condition a person has plays a significant role in their understanding—and risk perceptions—of safety issues with the medications they may take to treat these conditions.

Moderator's Comments and Closing Remarks

Video Segment: 11:50 - 12:00

Brian J. Zikmund-Fisher, PhD, Associate Professor of Health Behavior and Health Education, University of Michigan

Poster Session 4 and Break Topics

Poster Session 3 [Day 2, AM] [Patient and Consumer Engagement and Communication](#) (Pgs.155-169)

Afternoon Concurrent Session 7: Computational Modeling and Simulation at FDA

Session Chair: Grace Peng, PhD, Director of Computational Modeling and Simulation, National Institutes of Health/ National Institute of Biomedical Imaging and Bioengineering

Overview: Multi-scale Modeling in Biomedical, Biological, and Behavioral Systems

Video Segment: 0:00 - 9:23

Grace Peng, PhD, Director of Computational Modeling, Analysis, and Simulation, National Institutes of Health/National Institute of Biomedical Imaging and Bioengineering

Multi-scale modeling is making a significant impact in biomedical discoveries, applied science, and medicine. In 2004, the [Interagency Modeling and Analysis Group \(IMAG\)](#) released its first solicitation for multi-scale modeling of biomedical, biological, and behavioral systems. The IMAG Multi-scale Modeling Consortium (MSM) now has over 100 multi-scale modeling related projects. The MSM mission is to grow the field of multi-scale modeling in biomedical, biological, and behavioral systems.

Advancing Regulatory Science at FDA with Modeling and Simulation

Video Segment: 9:24 - 20:19

Tina Morrison, PhD, Chair, Modeling and Simulation Working Group, Center for Devices and Radiological Health

In its 2011 report, [Advancing Regulatory Science at FDA](#), the Agency identified an important role for modeling and simulation to support its regulatory science and strategic priorities. FDA identified eight regulatory science priority areas, four of which had identified a specific method or approach for modeling and simulation. This presentation gives an overview of the different types of modeling disciplines used for the different products that FDA regulates, at different phase of a product's lifecycle. It will also 1) showcase key projects on advancing regulatory science with modeling and simulation, 2) introduce the new FDA-wide working group on modeling and simulation, and 3) discuss our goals and objectives for advancing the role of modeling and simulation in regulatory decision-making.

Computational Electromagnetic Modeling and Medical Devices

Video Segment: 20:20 - 31:10

Leonardo Angelone, PhD, Research Biomedical Engineer, Center for Devices and Radiological Health

The [electromagnetic modeling \(EM\) group](#) in the [Office of Science and Engineering Laboratories](#) at CDRH supports the FDA regulatory and guidance role by advancing our knowledge of the complex interactions of EM fields with the human body. The research combines anatomically precise computational models and experimental measurements used in several areas of clinical significance. This work directly affects FDA's regulatory mission, since the tools developed by our research are extensively used by industry in pre-market evaluation for the safety and effectiveness of medical devices.

Using (Q) SAR Modeling to Inform Drug Safety Assessment

Video Segment: 31:15 - 42:24

Naomi Kruhlak, PhD, Chemist, Center for Drug Evaluation and Research

CDER supports the development and use of (quantitative) structure-activity relationship ((Q)SAR) models for regulatory decision-making through prediction of toxicity based on chemical structure. The Center's Chemical Informatics Program uses these models to predict the mutagenicity of drug impurities as a replacement for traditional testing and to provide supplemental toxicity predictions (e.g., carcinogenicity or liver damage) during regulatory safety review in the absence of adequate experimental data. More recently, (Q)SAR models that predict whether a synthetic street drug binds to opioid receptors have been developed to support the legal classification of newly identified substances. This presentation will provide an overview of (Q)SAR modeling at CDER, as well as supporting activities in database development and structure-based searching conducted by the Chemical Informatics Program.

Modeling the U.S. Blood Supply for Emergency Preparedness

Video Segment: 42:25 - 53:00

Mark Walderhaug, PhD, Microbiologist, Center for Biologics Evaluation and Research

To ensure a resilient blood supply in the nation, we developed a model of the U.S. blood supply to explore the variable effects of changes in the supply of blood resulting from pandemic or inter-regional disruptions that had an impact on blood donations. The model provides a simulation, from blood donation, to testing, to storage in blood collector inventories, to hospital inventory, and finally, to a patient. We have used the model to simulate the effect of a pandemic and the impact of changing the expiration date of stored blood on the blood supply.

Potential Uses for Modeling and Simulation in Veterinary Medicine

Video Segment: 53:02 - 1:05:20

Marilyn Martinez, PhD, Senior Scientist, Center for Veterinary Medicine (Presented by Bipin Mistry, MS, PhD, Clinical Pharmacologist/Expert Regulatory Scientist)

Unlike in human medical product review, there is no statutory requirement for pharmacokinetic data in new animal drug applications. As a result, there have been only a handful of examples where either nonlinear mixed effect pharmacokinetic models or *in silico* mechanistic modeling strategies have been included in new animal drug applications. Therefore, the Center for Veterinary Medicine is exploring the use and development of a range of M&S strategies. The goal is to continue refining these tools to optimize the efficiency of our product evaluation process and in so doing, encourage the submission of the therapeutic products needed to insure the health of companion and food-producing animal species.

Contamination of Food by Radionuclides after a Nuclear Accident

Video Segment: 1:05:22 - 1:16:12

Danielle Larese, PhD, ORISE Fellow, Office of Regulatory Affairs

This presentation discusses the use of computational modeling to increase the efficiency and rate of laboratory sample analysis following a nuclear accident. We propose combining map-based estimates of contamination, physics-based descriptions of permeation through packaging/food systems, and efficient modeling techniques to study radionuclide transport phenomena, to construct a sample triage mechanism. This may enhance sample targeting, therefore enabling a more efficient triage process. In addition, different laboratory analyses that require substantially less time may be used to sample categories with limited radionuclide permeability, enabling rapid information transfer to emergency response decision-makers.

Modeling and Simulation in Tobacco Regulatory Science

Video Segment: 1:16:15 - 1:29:23

Antonio Paredes, MA, MS, Lead Mathematical Statistician, Center for Tobacco Products

The Family Smoking Prevention and Tobacco Control Act (FSPTCA, Public law 111-31) grants authority to FDA to regulate tobacco products; it also gives FDA regulatory authority to regulate Modified Risk Tobacco Products (MRTP, tobacco products used to reduce harm or the risk of tobacco-related disease associated with commercially marketed tobacco products). FDA can authorize the marketing of a product as a MRTP only if the evidence submitted in an application meets the requirements of Section 911 of the FSPTCA. This talk presents several modeling and simulation strategies currently under development at the Center for Tobacco Products that could be used to investigate the impact of a new tobacco product on the population as a whole (i.e., taking into consideration users and nonusers), including agent-based models, system dynamic models, and social network analysis.

Q&A Session

Video Segment: 1:29:25 - 1:39:40

Poster Session 4 [Day 2, AM] Computational Modeling and Simulation at FDA (Pgs. 176-199)

Afternoon Concurrent Session 8: Current Progress in Nanotechnology Research at FDA

Session Chair: Anil Patri, PhD, Director, Nanotechnology CORE, National Center for Toxicological Research

[Current Progress in Nanotechnology Research at FDA \(NTF, CORES, Research Infrastructure Facilities\)](#)

Video Segment: 0:00 - 16:16

Anil Patri, PhD, Director, Nanotechnology CORE, National Center for Toxicological Research

Nanotechnology research is fueling development of novel nanomaterial-containing medical, food, and consumer products. FDA has established the [Nanotechnology Task Force \(NTF\)](#) to identify knowledge gaps, conduct research, train reviewers, develop guidance documents, and establish collaborative standards with this industry to facilitate responsible development of these technologies. This presentation will provide an overview of nanotechnology research at FDA and the advanced facilities available to conduct research relevant to regulated products.

[The Safety of Nanomaterials Using Silver Nanoparticles as an Example](#)

Video Segment: 16:22 - 31:23

Mary Boudreau, PhD, Research Toxicologist, National Center for Toxicological Research

The increasing number of food, cosmetic, and medical applications of silver nanoparticles (AgNP) and the general lack of toxicological and pharmacological data has raised public health safety concerns within the FDA. This prompted the nomination of AgNP for studies under the National Toxicology Program (NTP). A focus of this presentation will be the NTP studies conducted at NCTR and the approaches used to address the safety of silver AgNP.

Drug Products Containing Nanomaterials

Video Segment: 31:30 - 42:06

Katherine Tyner, PhD, Acting Associate Director of Science, Office of Pharmaceutical Quality, Center for Drug Evaluation and Research

The unique properties arising from the small size and large surface area of nanomaterials can result in additional scientific considerations when following current FDA guidelines and practices. Such considerations may extend to determining the correct analytical techniques to characterize and control the drug product. This presentation discusses the trends of drug products containing nanomaterials seen to date by FDA, scientific considerations, and current regulatory perspectives.

Nanotechnology and Medical Devices

Video Segment: 42:12 –57:10

Peter Goering, PhD, Research Toxicologist, Center for Devices and Radiological Health

The CDRH nanotechnology integrated program of research, standards, and health-based risk assessment has positioned CDRH to conduct better-informed review of products that incorporate nanotechnology. We address performance and safety concerns by characterizing the physico-chemical properties of nanomaterials associated with medical devices, evaluating the release of nanomaterials from devices, resolving biological testing issues (such as assay interference), and developing clinically relevant *in vitro* and *in vivo* models. Using a traditional toxicological risk assessment approach, we established a provisional tolerable intake level (a daily dose of chemical over time that does not pose appreciable harm to human health) for silver nanoparticles released from blood-contacting medical devices. Findings from these studies translate to international consensus standards and guidance documents for nanotechnology.

Nanomaterial-Based *In Vitro* Diagnostics for Pathogens

Video Segment: 57:20 - 1:09:47

Indira Hewlett, PhD, Laboratory Chief, Center for Biologics Evaluation and Research

Nanoparticles as novel nanomaterials are particularly attractive as probes or reaction substrates for rapid, ultrasensitive and multiplex detection of bio-analytes, due to their unique physiochemical properties. Our laboratory has shown that nanoparticle probes provide detection sensitivity limits in the sub-pg/mL range for the detection of HIV, influenza and anthrax lethal toxin antigens, and low copy number detection of genomes of HIV and influenza. The use of nanomaterials also facilitated the adaptation of assays to point-of-care formats such as microfluidic devices while maintaining good sensitivity and specificity. These studies will help identify potential problems in nanomaterial preparation and establish quality control processes for nanoparticle-based, *in vitro* devices for pathogen detection.

Potential Exposure to Nanoparticles from Nanotechnology-Enabled Food Contact Materials

Timothy Duncan, PhD, Research Chemist, Center for Food Safety and Applied Nutrition

Polymer nano-composites (PNCs) are materials in which nanoscale fillers are dispersed within a polymer host matrix. There is currently great interest in whether these composites will release nano-fillers into the nearby environment during product lifecycles. Our group studies potential exposure pathways using well-characterized model systems to investigate specific relationships between nano-filler characteristics and release kinetics. This talk presents several model systems developed in our laboratory, including ones that are based on semiconducting quantum dots or other nano-fillers. Our work shows that model systems are a powerful experimental complement to the use of commercial PNCs for lifecycle analysis of nanotechnology-enabled materials.

Panel discussion

Video Segment: 1:10:20 - 1:26:30

Anil Patri, PhD; Mary Boudreau, PhD; Katherine Tyner, PhD; Peter Goering, PhD; and Indira Hewlett, PhD

Closing Remarks and Adjourn

Carol Linden, PhD, Director, Office of Regulatory Science and Innovation