The 2019 FDA Science Forum

Transforming Health: Innovation in FDA Science

2019 Science Forum

Dates:	Sept. 11-Sept. 12, 2019
Location:	FDA White Oak Campus & Webcast
Focus:	Novel science and technologies that inform FDA's regulatory decision-making and drive innovation, such as new predictive tools for developing and evaluating therapeutics, advancing artificial intelligence, evaluating digital health devices, and novel methods of tackling critical public health challenges like addiction.
Goal:	Showcase research at FDA and generate collaboration with industry and academic laboratories to close FDA knowledge gaps and drive innovation in the regulatory science enterprise.
Attendance:	Sept. 11: 1036 (Webcast & on site) Sept. 12: 625 (Webcast & on site)

Link to electronic meeting book: https://www.fda.gov/science-research/about-science-research-fda/fda-science-forum

Link to agenda: https://www.fda.gov/science-research/fda-science-forum/2019-fda-science-forum-agenda

September 11, 2019 – Day 1

Introductory Presentations

Introduction

Rokhsareh Shahidzadeh, MSN
Video Segment: 0:00 – 2:08

Welcome

FDA Chief Scientist, RADM Denise Hinton
Video Segment: 2:10 – 14:00

Opening Remarks

Amy Abernethy, MD, PhD, FDA Principal Deputy Commissioner
Chief Information Officer
Video Segment: 14:03 – 24:30

Keynote Speaker

Francis Collins, MD, PhD, Director, National Institutes of Health
FDA and NIH: Partners in Transformation
Video Segment: 24:38 – 1:05:48

DAY 1 Presentations: September 11, 2019

Morning Concurrent Session 1: PRECISION HEALTH

Session Chair: Rhonda Moore, PhD, CDER-FDA

Introduction

Rhonda Moore, PhD, CDER-FDA
Video segment: 00:00 – 03:12

Regulatory Perspective on Digital Health for Precision Medicine

Bakul Patel, MSEE, MBA, CDRH-FDA
Video segment: 03:13 – 18:28

While precision medicine as a health care strategy continues to evolve with early areas of impact, significant challenges stand in the way of its fully disruptive potential. This talk provides an overview of digital health and precision medicine at the FDA, including a review of opportunities and barriers and real-world examples. To facilitate the introductions of smart, interconnected, personalized digital health devices, FDA launched a digital health software precertification pilot program (Pre-Cert). FDA also provided an overview of a novel, proposed regulatory framework for digital health, including Excellence Appraisal (EA) and Pre-Cert, Review Pathway Determination (RD),

Streamlined Review (SLR) and Real-World Performance (RWP). It emphasized regulatory and policy efforts for personalized artificial-intelligence- and machine-learning-based digital health devices.

Sex and Gender Differences in Health and Disease

Beverly Lyn-Cook, PhD, NCTR-FDA
Video Segment: 19:10 – 33:33

Sex differences in the epigenetic regulation in drug metabolizing and transporting enzymes can be key to individual responses to drugs. This laboratory, which was the first to investigate epigenome-wide methylation in normal human kidney tissue, identified sex-specific epigenetic variations. The work produced a reference methylome for normal kidney that may be used to improve understanding of renal disease and assess overall safety and effectiveness of drugs in the kidney.

Clinical Trials in 200 Microliters-Extending Approval in Rare Diseases Using In Vitro Data

Jim Weaver, PhD, CDER-FDA
Video segment: 33:06 – 48:56

Single-gene disorders such as cystic fibrosis (CF) and Fabry's Disease (FD) can be caused by any of hundreds of different variants, some of which are so rare that traditional clinical trials with appropriate numbers of participants are impossible. However, FDA was able to approve ivacaftor for CF and migalastat for FD, based on a small number of patients. This presentation explained how *in vitro* cell assays developed by the drug sponsors to produce data on the responsiveness of variant gene products not studied clinically, provided FDA with sufficient data to expand approval of these drugs for patients with rare variants of CF and FD.

Genomic Biomarker Use in Cardiovascular Disease Clinical Trials

Oluseyi Adeniyi, PhD, PharmD, CDER-FDA
Video Segment: 49:31 – 1:00.25

Increasing the use of genomic biomarkers to select subsets of patient for clinical trials might enhance the efficiency of cardiovascular drug (CVD) development. This talk reviewed how genomics has been applied in drug development, as well as recently-published findings evaluating the prospective use of biomarker in trials for CVD and related conditions that underscore potential opportunities for targeted drug development.

Learning Healthcare Systems and Big Data: Advancing the Goal of Precision Pain Medicine

Sean Mackey, MD, PhD, Stanford University
Video Segment: 1:01:04 – 1:34:59

CHOIR (http://CHOIR.stanford.edu, Stanford University) is an open source and free platform that represents an application of the digitally-based Learning Healthcare Systems (LHS) approach to medicine. This presentation describes CHOIR use in the cases of chronic pain and the perioperative experiences. Key topics include 1) clinical decision support features of CHOIR; 2) obtaining research-grade clinical data as a part of routine clinical care; 3) using LHS for clinical trials and rapid piloting of clinical interventions; 4) real-time aggregation and summarization of LHS data to provide on-going decision support in the perioperative and outpatient environments; 5) research efforts and publications made possible by large-scale LHS platforms like CHOIR.

Panel Discussion/Q&A

Bakul Patel, Beverly Lyn-Cook, Jim Weaver, Oluseyi Adeniyi, Sean Mackey
Video Segment: 1:35:15 – 2:02:45

Morning Concurrent Session 2: ADVANCED TECHNOLOGY

Session Chair/Moderator: Darón Freedberg, PhD, CBER-FDA

Accelerating Innovation in Manufacturing Technology for Bio-manufactured Products: Manufacturing US and NIST

Kelly Rogers, PhD, NIST
Video Segment: 0:01:22 – 25:43

Getting promising biologically manufactured therapies from the research bench to the bedside of the greatest number of patients at the least cost, requires the ability to produce these products with consistent quality and at appropriate scale.This presentation explored the contribution of the U.S. Metrology Institute at the National Institute of Standards and Technology to the rigorous evaluation of such products and its partnership with Manufacturing USA to build the skilled workforce needed for this growing industry. It also included the contributions of the National Institute for Innovation in Biopharmaceuticals and BioFabUSA in responding to the manufacturing challenges posed by complex products, such as cellular and gene therapies.

MetagenomeTrakr Pilot Program for Rapid Foodborne Pathogen Detection

Paul Morin, PhD, ORA-FDA
Video Segment: 0:26:20 – 42:50

This presentation discusses the potential for metagenomics to provide accurate, unbiased data about an entire microbial community, including pathogens, commensals, and organisms that cannot be cultured using traditional methods. The MetagenomeTrakr pilot project investigates the microbiomes of seafoods from various countries and environmental swab culture enrichments from food manufacturing facilities. Metagenomic DNA is extracted using mechanical lysis, which enables purification of high-quality microbial community DNA. Both 16S rRNA amplicon and shotgun metagenomic sequencing are used to analyze these samples and to compare results with traditional culture-based sampling methods. The data from this project will be publicly available in the MetagenomeTrakr Bioproject at the National Center for Biotechnology Information (NCBI).

The Promise of Microbial Genomics: How Microbiology is Standing Up to the Many Challenges of a 21st Century Food Supply

Marc Allard, PhD, CFSAN-FDA
Video Segment: 0:43:10 – 1:00:30

This talk described GenomeTrakr, FDA's integrated pilot network of laboratories that uses whole genome sequencing (WGS) to enhance traceback of foodborne pathogens to specific farms, facilities, and specific geographic areas. The network, which comprises several government food safety agencies and nearly three-dozen state, academic, and international partners, is creating a publicly available, global database containing the genetic makeup of tens of thousands of foodborne disease-causing bacteria, including *Salmonella*. FDA's Foods Program uses WGS to: 1) support trace back during foodborne contamination events; 2) enhance regulatory casework for high-risk commodities and compliance standards; 3) perform quality assurance of food microbiological sampling programs.

Editing the Genome without DNA Breaks

Jakob Reiser, PhD, CBER-FDA
Video Segment: 1:00:50 – 1:14:10

Gene therapy approaches involving genome editing tools, including engineered nucleases to introduce DNA double-strand breaks (DSBs), can cause unintended mutations—a major clinical concern. This presentation discusses

genome editing strategies investigated at FDA that do not require DSBs; instead they exploit the ability of strand-specific DNA nickases and of catalytically inactive Cas9 proteins to precisely target specific genomic sequences, while also delivering additional functional domains. FDA is also investigating site-specific recombinases for genome editing, which typically does not provoke error-prone DNA repair processes that result in insertions and deletions and is not dependent on the endogenous cellular DNA repair machinery.

Computational Modeling for Medical Devices

Pras Pathmanathan, PhD, CDRH-FDA
Video Segment: 1:14:28 – 1:31:09

Computational models are being used within software platforms, serving as clinical decision support tools, and are being embedded in medical devices. One major goal is clinical trial reduction using *in silico* clinical trials, where a device is tested on a cohort of virtual patients. This presentation provides an overview of the research and initiatives at CDRH that support the use of computational modeling and simulation (M&S) for medical devices.

Avian Influenza A Susceptibilities to Pulmonary Surfactant Protein D: Confirmation of N-glycan Sub-type as a Pathogenic Factor in Influenza

John Cipollo, PhD, CBER-FDA
Video Segment: 1:31:30 – 1:50:02

Seasonal Influenza Avian Virus carrying the key hemagglutinin (HA) head region high mannose glycans, can be removed from the lung by pulmonary surfactant protein D (SP-D), while those without these glycans cannot be. However, little is known about HA head glycosylation of low pathogenicity A type influenza virus (LPAIV) subtypes, which can pose a pandemic threat through reassortment. This presentation describes an investigation that reveals the glycan subtypes as complex at key head region glycosylation sites thought to interact with SP-D. As result, recombinant hn-SPD and rh-SP-D are not active against representative low pathogenicity LPAIV of different HA subtypes due to the presence of complex glycan subtype at these specific glycosylation sites.

Panel Discussion/Q&A: Potential Utility and Regulatory Challenges

Moderator: Glenn Black, PhD, CBER-FDA
Panel: Kelly Rogers, Paul Morin, Marc Allard, Jakob Reiser, Pras Pathmanathan, John Cipollo, Anil Patri
Video Segment: 1:50:10 – 2:05:19

Afternoon Concurrent Session 3: PRODUCT ACCESSIBILITY, INTEGRITY, and SECURITY

Session Chairs/Moderators: Leslie Rivera Rosado, PhD, CDER-FDA; Stephen Perrine, MS, CFSAN-FDA

Introduction: Product Accessibility, Integrity, and Security

Video Segment: 0:00:05 – 0:02:28

Violent Non-State Actor Use of Food as a Delivery System: Comparing Ideological and Non-Ideological Perpetrators

Marcus Binder, MA, University of Maryland
Video Segment: 0:02:34 – 0:24:00

Ideological and non-ideological perpetrators of violence who use chemical or biological agents choose distinctly different agents and tactics when using food as a delivery system. This presentation notes how these differences can affect threat likelihood, perpetrator characteristics and detectability, targeting choices, and potential for harm. Defense against such attacks must accommodate and respond to these two very different patterns of attack.

Product Availability: A Drug Shortage Perspective

Hyun J. Son, PharmD, CDER-FDA
Video Segment: 0:24:24 – 0:41:07

The CDER Drug Shortage Staff (DSS) oversees and facilitates temporary and long-term strategies to address shortages and coordinate timely and comprehensive risk/benefit decisions. DSS distributes up-to-date information daily via drug shortage web postings.

Bio-Terrorism Regulations and Food Security

Desmond Brown, DSc, ORA-FDA
Video Segment: 0:41:35 – 0:54:57

The Bioterrorism Act of 2002 requires the FDA to receive prior notifications of all imported food shipments before they arrive in the U.S. Using advanced, risk-based screening criteria, the Division of Food Defense Targeting (DFDT) identifies for manual review imported food shipments that may pose the highest risk for terrorism or other threats.During FY 2018, the FDA screened approximately 15 million Prior Notices (PN) against high-risk criteria and DFDT refused more than 600 imported food shipments for violations of PN data requirements.

FDA Food Defense Efforts-A Preventive Approach to Food Terrorism

Ryan Newkirk, PhD, MPH, CFSAN-FDA
Video Segment: 0:55:50 – 01:13:29

FDA, the food industry, academia, and other government partners collaborate in protecting the food supply from intentional adulteration. One of the major activities in this area has been the final rule "Mitigation Strategies to Protect Food Against Intentional Adulteration" stemming from the Food Safety Modernization Act. This presentation included a brief background of FDA's food defense efforts and requirements of the final rule.

CBER-Regulated Products: Preventing and Mitigating Shortages

Anita Richardson, MAS, CDER-FDA
Video Segment: 1:14:07 – 1:29:05

This talk reviews the statutory and regulatory requirements for notification of a permanent discontinuance or an interruption in manufacturing and the procedures for handling such shortage notifications. It also discusses CBER shortages and the tools CBER uses to prevent or mitigate shortages, and the center's engagement in the FDA Drug Shortage Task Force.

On the 'Cyber-Securability' of Medical Devices

Eugene Vasserman, PhD, Kansas State University
Video Segment: 1:29:40 – 1:37:45

FDA has designated security of medical devices in the context of deployment for intended use, as "securability." This definition of security is strictly stronger and more descriptive of real deployments than the current one referring only

to features introduced by manufacturers to protect devices and systems from attack, i.e., security features. This presentation discusses this concept of securability, and how a small, subtle shift in thinking about security requirement engineering and security feature implementation can be used to accelerate and simplify cross-stakeholder tasks (e.g., device handover, including documentation and on-site configuration) to improve security throughout the healthcare sector.

Panel Discussion

Moderators: Leslie Rivera Rosado, Stephen Perrine
Panel: Markus Binder, Hyun J. Son, Desmond Brown, Ryan Newkirk, Anita Richardson, Eugene Vasserman

Video Segment: 1:37:28 – 1:57:52

Afternoon Concurrent Session 4: PREDICTIVE TOOLS

Session Chair/Moderator: Donna Mendrick, PhD

Digital Biomarkers Discovery from Patient-Generated Health Data

Luca Foschini, PhD, Evidation Health
Video Segment: 0:00:00 – 0:26:45

Person-generated health data from wearable sensors, smartphone apps, and other IoT devices are high-frequency, continuously collected, and controlled by the individuals who generate them. This talk provided real-world examples of how these novel data streams can be used to develop techniques for measuring health, as well as diseases, such as influenza, diabetes, and cognitive decline. The talk showed how machine learning can help accelerate data analysis of person-generated health data, addressed needs around data quality and curation, and discussed considerations to enable successful implementation of trustworthy machine learning systems.

MRI in Nonclinical Safety Assessment

Serguei Liachenko, MD, PhD, NCTR-FDA
Video Segment: 0:27:00 – 0:42:54

A battery of known neurotoxicants with different mechanisms of action and pathology extent and localization were employed to test the ability of quantitative T_2 MRI mapping to noninvasively assess the neurotoxicity of investigational drugs in rats. Such imaging could be used as a supplement to guide current standard histopathology evaluations and has the potential to significantly modernize current approaches in neurotoxicity assessments in different areas, including drug discovery and development.

The VICTRE Project: The First All In Silico Imaging Clinical Trial

Aldo Badano, PhD, CDRH-FDA
Video Segment: 0:42:55 – 01:02:41

The VICTRE trial used computer-simulated imaging of *in silico* patients to compare digital mammography (DM) and digital breast tomosynthesis (DBT). The simulated trial was designed to replicate a clinical trial that used human patients and radiologists. It found an improved lesion detection performance favoring DBT for all breast sizes and lesion types. While further study of the generalizability of these findings is required, *in silico* imaging trials appear to be a source of regulatory evidence for imaging devices that could reduce the burden of regulatory evaluation.

Use of the MHC-Associated Peptide Proteomic Assay to Understand the Immunogenicity Risk of Therapeutic Proteins

Zuben Sauna, PhD, CBER-FDA
Video Segment: 1:02:47 – 1:16:38

This talk described the use of the MHC-Associated Peptide Proteomic (MAPPs) assay to study the immune response to Factor VIII replacement therapy in the treatment of hemophilia A. The MAPPs assay directly identifies peptides derived from a protein of interest on a donor's MHC-II proteins. The findings of this study showed that differences in the clinical immunogenicity of these products are consistent with the differences in the FVIII peptides found on the MHC-II proteins.

Cardiac and Hepatic Cellular Systems to Model Human Drug Effects

Alexandre Ribeiro, PhD, CDER-FDA
Video Segment: 1:16:48 – 1:37:39

The heart and liver are the main targets of drug adverse effects, and the field of drug development lacks cellular models that can better predict toxicity in these organs. Mammalian cells have the potential to model human physiology *in vitro* and can provide mechanistic insight on the clinical effects of drugs. However, lack of standardized quality control assays for cells used in engineered systems is the main roadblock in the field and should be the object of future research. This presentation provides insight into research aimed at tuning the microenvironment of stem cell-differentiated heart muscle cells (cardiomyocytes) and evaluating liver microphysiological systems. It demonstrates how engineering the microenvironment can improve the use of cellular systems in the regulatory field.

C. elegans for Rapid Developmental Neurotoxicity Assessment of Mixtures

Piper Hunt, PhD, CFSAN-FDA
Video Segment: 1:37:47 – 1:52:36

FDA scientists discussed their development of a novel worm Development and Activity Test (wDAT) that maps the timing of *C. elegans* developmental milestone acquisition as well as stage-specific activity levels. The wDAT detected both developmental delay and hyperactivity for arsenic, lead, and mercury--developmental neurotoxins that have been associated with hyperactivity in children. A planned 20-compound, blinded qualification study will help determine how the wDAT might provide "fit-for-use" data to support developmental neurotoxicity testing strategies.

Determination of Seafood Decomposition by Mass Spectrometry with Sensory-Driven Modeling

Randy L. Self, PhD ORA-FDA
Video Segment: 1:52:45 – 2:10:28

Sensory analysis to assess seafood decomposition is limited by the availability of qualified personnel and the need for extensive training, and complimentary methods (e.g., histamine or indole analysis) do not always produce results comparable to sensory analysis. Therefore, FDA developed and is studying two novel alternative techniques: 1) liquid-chromatography/high-resolution mass spectrometry with widely-focused sample extraction and instrumental conditions, and untargeted data-processing; 2) compact mass spectrometer with vapor-phase atmospheric pressure chemical ionization to test samples directly via headspace analysis. This talk reported on the results of tests that compared the accuracy of sensory analysis versus the two new FDA methods, and that showed promising results for both new methods.

Day 1 POSTERS SESSIONS

Poster Session 1

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Poster Session 2

Advanced Technology: Page 131
Product Accessibility, Integrity, and Security: Page 159
Predictive Tools: Page 175

Day 2 Presentations: September 12, 2019

Morning Concurrent Session 5: Advancing Digital Health and Artificial Intelligence

Session Chair/Moderator: Qi Liu, PhD/Richard Forshee, PhD

Welcome to Advancing Digital Health and Artificial Intelligence

Qi Liu, PhD, CDER-FDA
Video Segment: 0:00:00 – 0:04:30

Recent advances in artificial intelligence (AI) show great promise in improving the performance of existing medical devices, such as computer-aided diagnosis systems and novel applications, such as drug discovery and development of an autonomous "AI doctor" that continuously learns while deployed. Among the ways FDA can benefit from AI is by using natural language processing to comb through thousands of existing files from sponsors or social media to identify patterns of interest. This panel discusses these applications of AI, as well as regulatory challenges in reviewing AI-related submissions.

Deep Learning for Polypharmacy and Drug Repurposing

Marinka Zitnik, PhD, Stanford University
Video Segment: 0:04:40 – 0:45:01

This talk described a new methodology for large-scale predictive modeling of polypharmacy, a practice that poses a high risk of adverse side effects from drug-drug interactions. The project captured molecular, drug, and patient data for all drugs prescribed in the U.S. and developed deep learning methods that showed, for the first time, safety predictions and side effects of any drug combination. The new methods enable prediction of diseases a new drug can treat, give insights into mechanisms of their therapeutic effects, and predict effects of many repurposed drugs.

FDA's Real-World Evidence Program-Technology and Innovation as a Cornerstone

Jacqueline Corrigan-Curay, JD, MD, CDER-FDA
Video Segment: 0:46:00 - 1:06:50

The FDA framework for evaluating the potential use of real-world evidence (RWE) to help support the approval of a new indication for an approved drug, or to help support or satisfy post-approval study requirements, will require merging technologies, tools, and expertise. Machine learning and natural language processing could help organize and make sense of data from electronic health records (EHRs), which typically lack standardization. There is also great potential for using RWE in traditional randomized clinical trials, studies in health-care delivery settings, and observational studies. In addition, characterizing sources of data generated by digital tools such as sensors and mobile trackers to identify what is useful to measure a drug's effect on a clinical endpoint, is a challenge that requires collaboration with both the developers of these new technologies and clinicians.

Assessment of Devices that Rely on Artificial Intelligence/Machine Learning

Berkman Sahiner, PhD, CDER-FDA
Video Segment: 1:07:44 – 1:30:14

Artificial intelligence (AI) and machine learning (ML) techniques that automatically learn useful feature representations directly from data, has largely reduced or eliminated the need to engineer handcrafted features to interpret data. This has resulted in the proliferation of AI/ML-based systems that are considered "software as a medical device," (SaMD). The talk presented 1) examples of such devices recently approved/cleared/granted by CDRH; 2) current principles for evaluating these devices; 3) themes and challenges common to these applications, including limited training and test data sets, imperfect reference standards, and evolving algorithms; 4) a proposed regulatory framework for modifying AI/ML-based SaMD; 5) examples of FDA research that address some of these challenges.

Panel Discussion: AI at FDA: Potential Utility and Regulatory Challenges

Richard Forshee, PhD, CBER-FDA
Yaning Wang, PhD, CDER-FDA
Errol Strain, PhD, CVM-FDA
Rhonda Moore, PhD, CDER-FDA
Joshua Xu, PhD, NCTR-FDA
Jacqueline Corrigan-Curay, CDER-FDA

Video Segment: 1:29:23 – 2:03:11

Concurrent Session 6: **OUTBREAK!**

Session Chair/Moderator: Surender Khurana, PhD

Innovation in Science: Protecting People from Emerging Infectious Disease Threats

Christopher R. Braden, MD, Centers for Disease Control
Video Segment: 0:01:04 – 0:25:28

FDA and the Centers for Disease Control and Prevention (CDC) collaborate on surveillance and studies of medical products and procedures to advance the safety and efficacy of vaccines, blood transfusions, and organ and other tissue transplants. This collaboration also uses advances in detection and molecular characterization of pathogens to investigate foodborne outbreaks, hospital-associated infections, and antimicrobial-resistant pathogens. The two outbreaks of *E. coli* O157:H7 infections due to romaine lettuce in 2018 exemplified such collaborative investigations. The agencies also support advances in diagnostic and pharmacologic science by providing critical materials and information to scientists globally, including antimicrobial-resistant pathogens and materials from the AR Isolate Bank.

Foodborne Outbreak Investigations in the Whole Genome Sequencing Era

Jennifer Beal, MPH, CFSAN-FDA
Video Segment: 0:25:32 – 0:45:12

Nationwide, laboratories are phasing out Pulsed Field Gel Electrophoresis as the primary molecular subtyping tool for identifying outbreaks and replacing it with Whole Genome Sequencing (WGS), a much more sensitive and specific subtyping method. The use of WGS for foodborne outbreak investigations increases both the number of outbreaks detected (often with smaller numbers of cases per outbreak) and the number of outbreaks solved. This talk presented the FDA perspective on the impact of WGS on foodborne outbreak investigations. The talk summarized the current state of the WGS transition and made projections for the future of foodborne outbreak investigations and food safety in general.

Immune Responses to Zika Infections

Steven Wood, PhD, CDRH-FDA
Video Segment: 0:45:33 – 1:02:43

Zika virus (ZV) is a mosquito transmitted disease responsible for an outbreak of congenital microcephaly manifested recently in Brazil and the Caribbean. This presentation reviews technologies aimed at increasing the speed and specificity of Zika detection tests. A key challenge to test sensitivity is antibody cross-reactivity with other Flaviviruses (Dengue, West Nile, Chikungunya). Recent studies have focused on the evaluation rapid test methods of ZV, which has implications for diagnostics, vaccine development, and personal protection.

Tracking Antibiotic Resistance in Salmonella: The role of the National Antimicrobial Resistance Monitoring System

Patrick McDermott, PhD, CVM-FDA
Video Segment: 1:03:11 – 1:22:48

This presentation describes the National Antimicrobial Resistance Monitoring System (NARMS), an inter-agency program of FDA, USDA and CDC that tracks antibiotic resistance in foodborne bacteria from foods, animals, and human clinical cases. NARMS is establishing a One Health model of resistance monitoring that incorporates data on animal pathogens and environmental testing. It uses both genomic and metagenomic approaches to provide new insights into the ecology of antibiotic resistance. Interactive data displays are published online to make the data accessible to a broad audience. As NARMS is being reformed within the One Health model, it is moving towards real time data reporting and open data sharing to aid the global fight against antibiotic resistance.

Emerging & Pandemic Threat Preparedness

Jerry Weir, PhD, CBER-FDA
Video Segment: 1:23:10 – 1:38:57

Many recent emerging pandemic threats are caused by either zoonotic or vector-borne viruses, and in most cases, effective vaccines are not available. Recent examples include the threat of avian influenza virus, Ebola virus, and zika virus. In each case, research in the Division of Viral Products at the Center for Biologics Evaluation and Research played an important role in preparing for and responding to these threats.

Strengthening Regulatory Science to Support the Development of Medical Countermeasures for Emerging Infectious Diseases

Tracy MacGill, PhD, OC-FDA
Video Segment: 1:39:25 – 1:49:34

Panel Discussion
Session Chair/Moderator: Surender Khurana, PhD
Panel: Christopher R. Braden, Steven Wood, Patrick McDermott, Jennifer Beal

Video Segment: 1:50:28 – 2:07:17

Concurrent Session 7: Addiction

Session Chairs/Moderators: Katherine Bonson, PhD, Chad Reissig, PhD

Introduction
Kathrine Bonson, PhD, CDER-FDA
Video Segment: 0:00:00 – 0:01:15

The Controlled Substance Staff (CSS) at FDA works with drug sponsors to evaluate CNS-active drugs submitted under an investigational new drug (IND) application or a new drug application (NDA) for abuse potential. If there are abuse-related signals from nonclinical or clinical studies, it may be necessary to conduct two additional animal studies (drug discrimination and self-administration) and a human abuse potential study.If CSS concludes from an evaluation of the abuse-related studies that a drug has abuse potential, this will determine drug labeling in Section 9 (Drug Abuse and Dependence) and a recommendation regarding scheduling of the drug under the Controlled Substances Act (CSA).

Drug abuse in the US
Chad Reissig, PhD, CDER-FDA
Video Segment: 0:01:29 – 0:17:35

Drug overdose deaths in the US continue to increase, including deaths related to opioids (both licit and illicit), psychostimulants, and alcohol. This overview of addiction in the US, focuses on the primary drug classes of abuse (opioids, stimulants, depressants, alcohol and marijuana), highlighting the present state of addiction in the US. The presentation includes a brief overview of addiction, its definitions, and neurobiological mechanisms hypothesized to be involved in addiction; trends and changes in drug use, including opioids; the emergence of novel drugs of abuse. There is also an overview of the increased use of electronic nicotine delivery systems (ENDS).

FDA response to the opioid crisis
Marta Sokolowska, PhD, CDER-FDA
Video Segment: 0:18:05 – 0:37:03

Despite decreased prescribing, opioid abuse in the US still poses multiple challenges. At the same time, an estimated 25 million Americans experience pain every day. The many ways FDA is addressing the opioid crisis reflect the unique challenges of how opioids are used, misused and abused. This presentation summarizes the agency's current priorities and strategies. The key initiatives focus on decreasing exposure to prescription opioids and preventing new addictions, supporting the treatment of opioid use disorder, fostering the development of novel pain treatment therapies, and improving enforcement and risk-benefit evaluation.

Assessing the structural and pharmacological similarity of newly identified drugs of abuse to controlled substances using PHASE

Chris Ellis, PhD, CDER-FDA
Video Segment: 0:38:05 – 0:54:26

The emergence of new fentanyl derivatives on the street-drug market has led to a rapid increase in overdose deaths, attributable to their high potency and inexpensive synthesis. Slight chemical modifications to the parent drug evade control by national and international legislation and there are often little to no pharmacological and toxicological data available. FDA's Center for Drug Evaluation and Research (CDER) developed the Public Health Assessment via Structural Evaluation (PHASE) protocol, a multi-pronged computational approach that uses molecular structure to rapidly and systematically evaluate a drug's risk to public health in the absence of significant *in vitro* or *in vivo* data. PHASE has the potential to inform law enforcement agencies with vital information regarding newly emerging illicit opioids.

Preclinical pharmacology of novel synthetic opioids appearing in clandestine drug markets

Michael Baumann, PhD, National Institute on Drug Abuse-NIH
Video Segment: 0:54:56 – 1:17:08

There is a critical need for rapid and accurate pharmacological evaluation of novel synthetic opioids (NSOs) encountered in clandestine drug markets worldwide to inform the public and assess risks. This presentation described *in vitro* and *in vivo* (rodent) laboratory strategies to determine the potency and efficacy of NSOs, which include analogs of fentanyl and non-fentanyl compounds. *In vitro* methods include radioligand binding at opioid receptor subtypes and *in vivo* paradigms include analgesia testing. One important conclusion is that *in vitro* binding affinity of a drug at mu-opioid receptors does not always predict *in vivo* potency.

FDA assessment of the abuse potential of drugs

Katherine Bonson, PhD, FDA-CDER
Video Segment: 1:17:34 – 1:32:23

The Controlled Substance Staff (CSS) at FDA works with drug sponsors to evaluate CNS-active drugs submitted under an investigational new drug (IND) application or a new drug application (NDA) for abuse potential. If there are abuse-related signals from nonclinical or clinical studies, it may be necessary to conduct two additional animal studies (drug discrimination and self-administration) and a human abuse potential study.If CSS concludes from an evaluation of the abuse-related studies that a drug has abuse potential, this will determine drug labeling in Section 9 (Drug Abuse and Dependence) and a recommendation regarding scheduling of the drug under the Controlled Substances Act (CSA).

Panel Discussion

Chad Reissig, PhD
Mata Sokolowska, PhD
Chris Ellis, PhD
Michael Baumann, PhD
Katherine Bonson, PhD

Video Segment: 1:32:40 – 1:56:52

Concurrent Session 8: Impacting Public Health Through Electronic Media: Empowering Consumers, Patients, and other Stakeholders

Session Chair/Moderator: Ryan Kennedy, PhD

Tobacco Regulatory Science-Understanding the Role of Flavor in E-Cigarette Marketing

Ryan Kennedy, PhD, The Johns Hopkins Bloomberg School of Public Health
Video Segment: 0:03:00 – 0:19:39

This presentation surveyed advertising for electronic nicotine delivery systems (ENDS) to determine how they incorporated flavors. The researchers studied ENDS advertisements that ran during 2015, 2016 or 2017 and included direct-to-consumer mail, direct-to-consumer emails, magazines, and social media (such as banner posts). The study identified 1860 unique ENDS ads, most of which (66%) included a reference to flavor, the most common of which was tobacco (45%). Other flavors found in ads included menthol (32%), fruit/berry flavors (22%), spice/clove (11%), and mint (14%). Many ENDS products advertised (20%) featured unconventional flavor names, such as "Sweet Lava" and "Meteor Milk". Additional research about the effect of marketing on consumer behavior, and the monitoring of ENDS ads can help inform tobacco regulatory activities.

Using Content Analysis to Understand Tobacco Industry Use of Technology to Engage Consumers

Mario Navarro, PhD, Center for Tobacco Products-FDA
Video Segment: 0:19:52 – 0:33:30

This presentation describes how cigarette, smokeless tobacco, hookah, and Electronic Nicotine Delivery Systems [ENDS] companies reach people using smartphone-optimized (mobile) websites, apps, and social media. For example, most ENDS, hookah, and cigar brands had at least one social media page, while very few cigarette and smokeless brands did. Many pages contained links to branded websites and online stores, and pages' posts featured images of specific products. Few pages used any age gating, and less than one-quarter had a visible health warning. This information can inform tobacco regulatory activities and prevention and cessation interventions.

Consumers' Use of Personal Electronic Devices in the Kitchen

Amy Lando, MPP, FDA-CFSAN
Michael Bazaco, PhD, FDA-CFSAN
Video Segment: 0:33:40 – 0:46:59

This presentation discussed the use of data from the 2016 Food Safety Survey (FSS) and subsequent focus groups to determine the frequency of consumers using their personal electronic devices (e.g., smartphones and tablets) in the kitchen while preparing food, what type of devices they use, and their handwashing behaviors after handling their devices. Previous research has shown that cell phones can harbor bacteria including opportunistic human pathogens (such as *Staphylococcus* and *Klebsiella* spp.). The FSS found that of those who use personal electronic devices while cooking, only about a third reported washing their hands after touching their device before they continue cooking. This is significantly lower than the self-reported handwashing behavior after touching risky products such as raw meat, chicken, or fish.

Assessment of Patient Perspective on Risks and Benefits Associated with High Intensity Focused Ultrasound (Hifu) for the Ablation of Prostate Tissue in Men with localized Prostate Cancer

Charles Viviano, MD, PhD, FDA-CDRH
Olufemi Babalola, MHS, MSc, FDA-CDRH
Video Segment: 0:47:08 – 1:04:18

Patients and regulators must make decisions regarding High Intensity Focused Ultrasound (HIFU) for prostate ablation in U.S. men with prostate cancer with little cancer-specific clinical effectiveness data except for known potential adverse events and 12-month post-treatment prostate biopsy data. This presentation describes a proposed study of men who have been diagnosed with organ confined (localized) Gleason 6 or 7 prostate cancer who have not undergone any prostate cancer treatment. It is designed to collect patient perspectives on available benefit data or tolerance of risks that have been associated with HIFU for prostate ablation. Such information may inform future

premarket device evaluation of ablation tools and speed the development and availability of improved ablation devices.

Digital health technology tools (DHTTs) to assess clinical benefit

Elektra J. Papadopoulos, MD, MPH, FDA-CDER
Video Segment: 1:04:27 – 1:20:19

A digital health technology tool (DHTT) is an electronic technology tool (including scoring and interpretation) intended for use in clinical trials. DHTTs can include "wearables" (e.g., accelerometers), stationary sensors (e.g., home-based motion sensors to detect gait patterns and capture falls) and other tools. DHTTs can be used to assess existing endpoints remotely or to assess novel endpoints. This presentation introduces some of the regulatory considerations for endpoints derived using DHTTs for assessment of clinical benefit in medical product development.

Collect Once, Use Many Times: Challenges and Opportunities for the Use of Real-World Evidence to Improve Healthcare

Gregory Pappas, MD, PhD, CBER-FDA
Video Segment: 1:20:25 – 1:39:40

This presentation provides an overview of the Biologics Effectiveness and Safety (BEST) System at FDA's Center for Biologics Evaluation and Research (CBER). BEST promotes the use of data collected as part of routine clinical care (real world evidence, RWE) to support CBER's Office of Biostatistics and its mission to ensure the safety and effectiveness of biologic products. The objectives of BEST contracts are to: 1) build operational infrastructure and provide FDA with indirect access to large-scale US health care data, including administrative and claims and electronic health records data sources; 2) build the capability and capacity to run queries and observational studies on the data sources for CBER-regulated biologic products; 3) develop semi-automated processes for medical chart review to augment manual review of charts.

Panel Discussion

Moderator: Ryan Kennedy
Panel Members: Ryan Kennedy, Mario Navarro, Amy Lando, Michael Bazaco, Charles Viviano, Elektra Papadopoulos, Gregory Pappas

Video Segment: 1:39:50 – 1:56:51

Closing Remarks and Adjourn

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

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