CENTER FOR DRUG EVALUATION AND RESEARCH

What's New in Regulatory Science

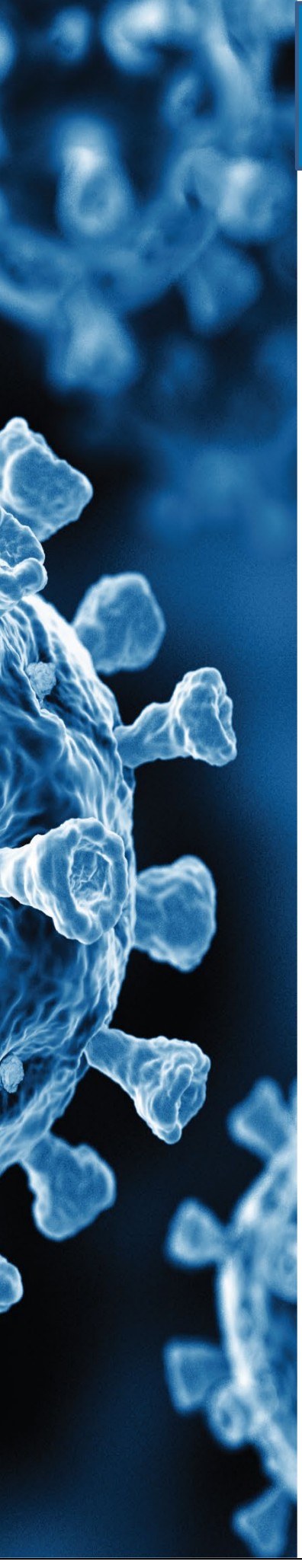
Issue III - 2022

CONTENTS

Brought to you by the Office of Translational Sciences (OTS) in collaboration with the Office of Communications within the Center for Drug Evaluation and Research (CDER)

What's New in Regulatory Science is a quarterly newsletter from the Food and Drug Administration's (FDA's) Center for Drug Evaluation and Research (CDER). It features new developments, opportunities, and initiatives in drug development regulatory science, with the goal of advancing medical product development.

Please share this message and the sign-up link with colleagues (Select Regulatory Science as the Topic Area). If you have comments or questions, please contact us at OTSCommunications@fda.hhs.gov.



COVID-19- RELATED EFFORTS

The FDA is engaged in numerous activities to protect and promote public health during the COVID-19 pandemic. For CDER, these efforts include accelerating development of treatments for COVID-19, maintaining and securing drug supply chains, providing guidance to stakeholders, advising developers on how to handle clinical trial issues and keeping the public informed. Previous updates on some of CDER's efforts related specifically, to drugs and COVID-19 can be found in the 2020 and the 2021 issues of the newsletter (click here to access the 2020 and 2021 issues) and in the webpages below:

- Coronavirus (COVID-19) Drugs Web Page
- FDA's Work to Combat the COVID-19 Pandemic
- FDA updates on hand sanitizers consumers should not use
- COVID-19 Health Care Professional Resources

Some recent updates are provided below:

COVID-19 APPROVALS, EMERGENCY USE AUTHORIZATIONS AND UPDATES

FDA announces that bebtelovimab is not currently authorized in any U.S. region

November 30, 2022: FDA announced that bebtelovimab is not currently authorized for emergency use in the U.S. because it is not expected to neutralize Omicron subvariants BQ.1 and BQ.1.1. *Learn more.*

FDA releases important information about risk of COVID-19 due to certain variants not neutralized by Evusheld

October 3, 2022: FDA added important information to the authorized Fact Sheet for Evusheld (tixagevimab co-packaged with cilgavimab) to inform health care providers and individuals receiving Evusheld of the increased risk for developing COVID-19 when exposed to variants of SARS-CoV-2 that are not neutralized by Evusheld. Learn more.

FDA provides additional guidance for evaluation of potential drug interactions for Paxlovid therapy for COVID-19

August 26, 2022: FDA provided additional guidance to help prescribers evaluate potential drug interactions when using Paxlovid therapy for COVID-19. Please see the updated Prescriber Patient Eligibility Screening Checklist for more information.

REGULATORY SCIENCE IN ACTION

November 16, 2022. FDA releases a report, "Successes and Opportunities in Modeling and Simulation for FDA"
Computational (in silico) modeling and simulation (M&S) are powerful tools that complement traditional methods for gathering evidence about products regulated by the Food and Drug Administration (FDA) or for developing FDA policy. This report describes the role and impact of M&S across the Agency. Learn more.

October 6, 2022: **FDA Launches AATD Pre-Consortium Partnership with the Critical Path Institute**
FDA's Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER) are pleased to announce their partnership with the Critical Path Institute (C-Path) to initiate planning for a consortium aimed at developing tools appropriate for use in clinical development programs for alpha-1 antitrypsin deficiency (AATD), a rare disease-causing progressive destruction of lung tissue leading to premature mortality or need for lung transplant. Learn more.

September 14, 2022: FDA and NIH Launch Public-Private Partnership for Rare Neurodegenerative Diseases
The U.S. Food and Drug Administration and the National Institutes of Health (NIH) announced the launch of the Critical Path for Rare Neurodegenerative Diseases (CP-RND) – a public-private partnership aimed at advancing the understanding of neurodegenerative diseases and fostering the development of treatments for amyotrophic lateral sclerosis (ALS) and other rare neurodegenerative diseases. Learn more.

September 6, 2022: **FDA Publishes the 2022-Advancing Regulatory Science at FDA**
The FDA published the 2022: Advancing Regulatory Science at FDA: Focus Areas of Regulatory Science (FARS) report, which outlines topics the agency has identified as needing continued targeted investment in regulatory science research to facilitate the development of innovative products, provide data and methods to inform regulatory decision-making and improve guidance to sponsors. This research facilitates evaluation or development of FDA-regulated products and supports regulatory decision-making and policy development. It also enables the FDA to understand and assess risk, prepare for, and respond to public health emergencies, and help ensure the safety or reduce the harm of products used or consumed by patients and consumers. The 2022 report expands on cross-cutting topics and includes research, achievement and progress updates for focus areas included in the inaugural 2021 report.

May 23-24, 2022: International 2022 Drug-Induced Kidney Injury Biomarker Workshop Report:
This workshop was held in May 2022 over two days (day one video and day two video) with more than 250 registrants from academia, industry, and regulatory agencies. Industry participants described how the novel kidney injury biomarkers have been incorporated into

their early clinical trials for drug development decision making such as compound selection and dose escalation. The workshop attendees agreed was that there is a need for data sharing of safety biomarkers to facilitate collective learnings and use in clinical research and drug development. The attendees also suggested pathways for sharing biomarker data and their use in drug development through a central data repository such as C-Path's Biomarker Data Repository (BmDR).

As a direct result of the Planning and discussions for the DIKI during the workshop, to date, two companies agreed led to the sharing of four clinical data sets of data. These four data sets, in addition to These plus the PSTC normal healthy volunteer studies, form the foundation to expand the patient populations (e.g., diabetic, obesity, cancer, etc.) where novel kidney injury biomarkers may be used in drug development. This will be accomplished by determining the normal reference range and the thresholds of concern or injury within each patient population. An additional outcome from the workshop is that more researchers are interested in sharing their clinical novel kidney injury biomarker data to expand the database for new contexts of use and regulatory endorsement.

REGULATORY SCIENCE IMPACT STORIES

Assessing the Impact of Opioid Overdose and Naloxone Dosing to Support Medical Product Development

Although naloxone products can be administered to people experiencing opioid overdose by those without extensive medical training, developing dosing guidelines is challenging. CDER researchers constructed a mathematical model that provides regulators with a robust framework for assessing the ability of naloxone formulations and dosing to reverse opioid overdose in a community setting, including for emerging synthetic opioids. The model faithfully reproduced clinical outcomes and has supported approval of a naloxone hydrochloride injection product as an emergency treatment for individuals over aged 12 years of age in whom high-potency opioid use is suspected. Learn more.

How should risk information be conveyed in online ads with space limitations: results from CDER's randomized study?

The rise of Internet communications that have character space limitations, such as Tweets and Google-sponsored links, has led to questions about how to use these communications for prescription drug promotion while ensuring that risk information is adequately conveyed. Some stakeholders have suggested that simply including a link to risk information in these space-limited communications may be sufficient. CDER researchers addressed this and other questions about how to ensure that viewers fully understand the benefits and risks of drugs promoted in space-limited drug ads. The findings from their randomized study in nearly 2000 participants can help us develop regulations that ensure that ads are designed so that the public is fully informed of the potential benefits and risks of the drugs they learn about online. Learn more.

SPOTLIGHT ON CDER SCIENCE

Assessing the Respiratory Effects of Approved Opioid Products When Co-administered with Commonly Prescribed Drugs

Some drugs, such as benzodiazepines, can further decrease the respiratory response to low levels of carbon dioxide when used in combination with opioids and in 2016, the FDA required safety labeling changes, for benzodiazepine and opioid products, to indicate that their combined use could increase the potential for respiratory depression. The agency then undertook a multi-step approach to assess whether drugs other than benzodiazepines might also raise the potential risk for respiratory depression when co-administered with opioids. Most recently, FDA has conducted a clinical trial to assess whether paroxetine or quetiapine, which FDA investigators had shown to increase the risk of respiratory depression when combined with opioids in animal studies, would have similar effects in humans. They found that that paroxetine combined with oxycodone compared with oxycodone alone decreased the hypercapnic ventilatory response with concentration-response modeling showing the effects of the drugs in combination were outside the range of effects modeled by variation of oxycodone concentration alone. The clinical study serves as a proof-of-concept for how this methodology could be prospectively used for evaluating effects of investigational drugs alone or in combination with other drugs on ventilation. Learn More.

IN PRESS

This section provides highlights of select CDER research recently published in scientific journals. Click here to see the complete FDA publication list. To view CDER publications on this site, select Drugs under the Centers category

Roadmap to 2030 for drug evaluation in older adults

CDER experts discuss deficits in the current conduct of clinical evaluation of drugs for older adults and steps that should be taken to address this issue, the most of important of which is to increase clinical trial enrollment of older adults who are representative of the target treatment population. Learn more.

Optimization of screw design for continuous wet granulation: a case study of metoprolol succinate ER tablets

Granulation of powdered particles to form larger agglomerates is a critical step in forming drug tablets, capsules, and other dosage forms. CDER researchers and collaborators report on research to optimize design parameters in the process of twin screw granulation for producing extended-release tablets via a continuous manufacturing approach. Learn more.

Recommendations for achieving Interoperable and shareable medical data in the USA

CDER scientists and external collaborators provide recommendations for developing standardized data collection and exchange practices that can support medical research, epidemiologic surveillance during pandemics, and medical product regulation while allowing us to achieve an analytical information environment that best serves the needs of patients. Learn more.

Scientific and regulatory activities initiated by the U.S. Food and Drug Administration to foster approvals of generic dry powder inhalers

In separate papers, CDER scientists review challenges in developing generic versions of dry powder inhalers (DPIs). The first review focuses on Chemistry, Manufacturing and Controls (CMC) for generic DPI quality attributes and provides recommendations to ANDA applicants to expedite approvals. A second review furnishes recommendations for establishing bioequivalence to the reference product and describes novel in vitro and in silico methods that may be useful to developers.

CDER- RESEARCH AREAS, TOOLS AND TRAININGS

1. CDER's Regulatory Science Program Areas

CDER's diverse research programs address a wide variety of critical areas that affect drug safety and manufacturing quality. Learn more at https://www.fda.gov/drugs/science-and-research-drugs/cders-regulatory-science-program-areas

2. Research Tools and Resources

Developing and sharing knowledge with researchers from the public and private sectors is at the heart of what Center for Drug Evaluation and Research (CDER) scientists do. Learn more about scientific tools and resources at CDER/FDA at https://www.fda.gov/drugs/science-and-research-drugs/research-tools-and-resources

3. Office of New Drugs Regulatory Science Research

The Office of New Drugs (OND)-led regulatory science research projects are designed to address knowledge gaps identified during regulatory review of investigational or new drug applications. Learn more about the research programs at https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/office-new-drugs-regulatory-science-research

4. CDER/CDER Learn Training and Education

Information on learning opportunities for healthcare professionals, academia, students, and consumers can be accessed at https://www.fda.gov/Training/ForHealthProfessionals/default.htm

CAREER OPPORTUNITIES

You want to make a difference.

FDA wants to hire You.

Employment

FDA continues to recruit and retain a world-class workforce dedicated to protecting and promoting public health. Information on job vacancies, employment events, and hiring programs can be found by following @FDAJobs on Twitter and by visiting FDA's LinkedIn page, Jobs at CDER, or the Career Opportunities at CDER webpage. In addition, you can contact OTS directly at CDEROTSHires@fda.hhs.gov. Help us spread the news through your social media networks!

Scientific internships and fellowships

Whether you're an undergraduate looking to pursue a career in science, a graduate student seeking experience in regulatory science, a postgraduate looking for fellowship opportunities, or a senior scientist pursuing research experience in your field of expertise, FDA offers you many paths to learning about the exciting field of regulatory science. Click here for more information.

FDA-NCATS Translational Science Interagency Fellowship (TSIF)- Submission deadline- January 20, 2023

The Translational Science Interagency Fellowship (TSIF) program is jointly sponsored by NCATS and the U.S. Food and Drug Administration (FDA) and aims to provide training in both translational science and regulatory science. The application cycle started on September 19, 2022. Submit your applications by **January 20, 2023**. Learn more.