CENTER FOR DRUG EVALUATION AND RESEARCH

What's New in Regulatory Science

Issue I- 2024

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 and 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.

REGULATORY SCIENCE IN ACTION

April 15, 2024: FDA Establishes CDER Center for Clinical Trial Innovation (C3TI)

FDA's Center for Drug Evaluation and Research (CDER) has recently launched the CDER Center for Clinical Trial Innovation (C3TI). C3TI is a central hub that supports innovative approaches to clinical trials that are designed to improve the efficiency of drug development. C3TI aims to promote existing CDER programs and spur future innovation activities through enhanced communication and collaboration. C3TI will enable internal and external parties to access information more easily, engage in collaborations, identify resources that can further support the use of innovative modalities, and find development programs where a concerted approach to the use of clinical trial innovations would be impactful. Learn more.

February 8, 2024: In a Parallel Scientific Advice Pilot Program for Complex Generics CDER OGD and the EMA Seek to Increase Harmonization and Bring Generic Drugs to Patients

CDER's Office of Generic Drugs (OGD) and the European Medicines Agency (EMA) launched a voluntary pilot program to facilitate concurrent discussions between generic drug applicants and the two regulatory bodies, with a goal of improving patient access to harder to develop generic drugs. Learn more.

February 2024: CDER's Division of Applied Regulatory Science shares its annual report.

The *2023 DARS Annual Report* features the Division's accomplishments from the past year, including landmark applied research studies. Because 2023 marked the 10-year anniversary of the Division, this year's issue features a review of DARS' growth and accomplishments over the past decade. Looking to the future, the report also highlights the Division's 3-year strategic plan and roadmap, which seeks to set standards for applied research and build a sustainable infrastructure to support quality. Learn more.

Annual reports on scientific Progress from other CDER Offices and Divisions have been published recently. Learn more.

January 23, 2024: FDA's ISTAND Pilot Program accepts submission of first artificial intelligence-based and digital health technology for neuroscience.

FDA's Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER) recently accepted a new submission into the Innovative Science and Technology Approaches for New Drugs (ISTAND) Pilot Program. This submission is the first artificial intelligence-based and digital health technology-based project and the first project in neuroscience to be accepted into ISTAND. Learn more.

January 21, 2024: Artificial Intelligence Paper Outlines FDA's Approach to Protect Public Health and Promote Ethical Innovation

The U.S. Food and Drug Administration (FDA) released its "Artificial Intelligence and Medical Products: How CBER, CDER, CDRH, and OCP are Working Together," which outlines how FDA's medical product centers are working together to protect public health while fostering responsible innovation in artificial intelligence (AI) used in medical products and their development. Learn more.

January 2024: FDA releases the Revised Biosimilar User Fee Amendment (BsUFA) Research Roadmap

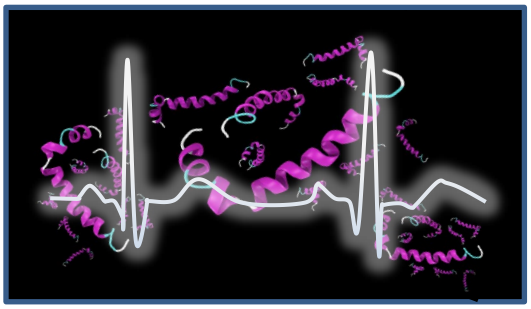
FDA releases the Revised Biosimilar User Fee Amendment (BsUFA) Research Roadmap to provide updated information about the biosimilar regulatory science research pilot program research priorities. Learn more.

REGULATORY SCIENCE IMPACT STORIES

Deep Learning-enabled Natural Language Processing to Identify Directional Pharmacokinetic Drug-Drug Interactions

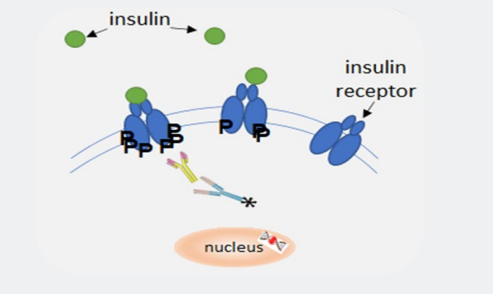
CDER researchers report on their development of a publicly available AI-based tool that can 1) automatically identify drug-drug interactions that lead to significantly higher or lower patient exposure in free text and 2) identify the directionality of the interaction, i.e., which of the interacting drugs causes the problematic exposure. The tool, BioBERT_directionalDDI, is based on-the pre-trained large language model BioBERT and fined tuned on labeling information. It could be used in specific drug development programs when the drug of interest has relevant information in other drug labels or scientific literature. Natural text mining using this tool could also be used for post marketing pharmacovigilance surveillance for specific drugs. Learn more.

A CDER Study Suggests that for Peptides and Proteins Clinical Studies of the Product' s Effect on the QT Interval are not Needed



CDER investigators reviewed information on peptide and protein products submitted to the FDA and found that the hERG potassium channel and ventricular repolarization assays did not identify clinical QTC prolongation potential for intermediate sized molecules. The investigators concluded that peptides and proteins regardless of size have a low likelihood of direct cardiac ion channel interactions and that this supports waiving the requirement for thorough QT assessment for products comprised of naturally occurring amino acids unless proarrhythmia potential is suggested by nonclinical or clinical data. Learn more.

An in-vitro Cell-based Assay to Assess the Biological Activity of Insulin Products



CDER researchers have established and validated an in vitro insulin cell-based assay, derived from the USP chapter <121> “insulin assays,” to expand the ability to assess the biological activity of insulin glargine, insulin aspart, and insulin lispro in vitro. This method is easily performed with commonly used equipment and amenable to adaptation for assessing the biological activity of other insulin analogs. Details of the method are published in an open access journal to provide a methodological option to drug developers and regulators with interests in assessing the biological activity of insulin analogs. Learn more.

How Physicians Interpret Information about Prescription Drugs in Scientific Publications versus Promotional Pieces

To better understand how physicians process and interpret information that could guide prescribing, and how such factors as time pressure, whether the information source is promotional in nature, and indicators of methodological rigor may influence physician’s perceptions of a drug product and prescribing, CDER researchers conducted a randomly controlled study among primary care physicians. One implication of this study’s results is that non-traditional forms of advertising like native advertising may pose a significant risk of being undetected by physicians and other healthcare providers as true “promotion” and thus be approached with less caution. Learn more.

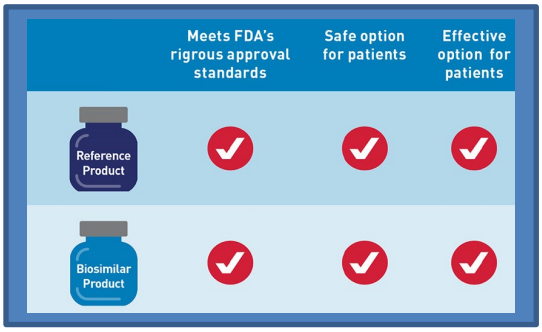
SPOTLIGHT ON CDER SCIENCE

Sociodemographic Characteristics of Adverse Event Reporting

A recent Spotlight on CDER Science describes research examining the sociodemographic characteristics (such as age, sex, race, and ethnicity) of individuals who submit reports to the FDA Adverse Event Reporting System (FAERS) through the MedWatch program. The results showed that sociodemographic factors are associated with different levels of reporting. Specifically, the study highlighted that adverse events in some populations may be under-reported, which may affect the ability of FAERS to detect certain safety signals.

This study showed that adverse event reporting data, while valuable, may not fully capture the experiences of the entire population using the drug. It is important that we continue to help populations whose adverse events are under-reported understand the value of the surveillance system and encourage them to report events to the MedWatch program. Learn more.

CDER Research Focuses on Biosimilar "Switching"



In this Spotlight on CDER Science, FDA researchers conducted a systematic review and meta-analysis using statistical methods to determine whether there were safety outcome differences between individuals who switched between a biosimilar and a reference product and individuals who did not switch. The researchers concluded that there were no differences in the risk of death, serious adverse events, or treatment discontinuations between the switch and no-switch arms. These findings are consistent with previously published non-statistical descriptive reviews of switching biosimilars. They provide additional evidence for patients and their health care professionals that switching between biosimilars and their reference products is not associated with major safety events. Learn more.

IN PRESS

This section provides highlights of select CDER research recently published in scientific journals.

Characterizing a design space for a twin-screw wet granulation process: a case study of extended-release tablets

CDER's study of twin-screw wet granulation demonstrates that simultaneous optimization of both operating and screw design parameters is beneficial in producing extended-release granules and tablets of desired performance characteristics while mitigating failure risks. Learn more.

Utility of PBPK to Investigate the Impact of Physiological Changes of Pregnancy and Cancer on Oncology Drug Pharmacokinetics

FDA Investigators describe and report results from a pharmacokinetic modeling framework for predicting exposures of oncology drugs in women who are pregnant. Learn more.

Determining topical product bioequivalence with stimulated Raman scattering microscopy

CDER investigators report on their development of an approach based on Simulated Raman Scattering Microscopy for the evaluation of topical product bioavailability and bioequivalence in excised human skin. Learn more.

Morphologically Directed Raman Spectroscopy as an Analytical Method for Subvisible Particle Characterization in Therapeutic Protein Product Quality

CDER researchers applied a method based on Morphologically Directed Raman Spectroscopy to identify and characterize subvisible particles in protein therapeutics. The analytical approach may have the potential to improve our capacity to detect these potentially harmful impurities. Learn more.

Methanol poisonings from contaminated hand sanitizers identified by the United States Food and Drug Administration

The actions and analyses and actions taken by an FDA task force to address methanol poisoning following intentional alcohol-based hand sanitizers ingestion are summarized in this letter to the editor of *Clinical Toxicology*. Learn more.

CDER- RESEARCH AREAS, TOOLS AND TRAININGS

FDA's Regulatory Science

Regulatory Science is the science of developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of all FDA-regulated products. Learn more at https://www.fda.gov/science-research/science-and-research-special-topics/advancing-regulatory-science and Researching FDA – YouTube.

FDA: Overview of our Role Regulating and Approving Drugs | Video Series

FDA oversees prescription, generic, biosimilars, and over-the-counter drugs. Learn more at Overview of our role regulating and approving drugs | Video series | FDA.

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.

Research Tools and Resources

Developing and sharing knowledge and scientific resources with researchers in the public and private sectors is at the heart of what 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.

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 these research programs at https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/office-new-drugs-regulatory-science-research.

Office of Generic Drugs- Science and Research

The Office of Research and Standards within the FDA's Office of Generic Drugs (OGD) supports the Science and Research program established under the Generic Drug User Fee Amendments (GDUFA). In collaboration with industry and the public, FDA creates an annual list of its regulatory science initiatives on generic drugs. Learn more at https://www.fda.gov/drugs/generic-drugs/science-research.

CDER- Training and Education

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

UPCOMING EVENTS

Information on upcoming meetings, conferences, and workshops sponsored or co-sponsored by CDER, click here. Some of the events are listed below:

- **May 20-21, 2024: Fiscal Year 2024 Generic Drug Science and Research Initiatives- Public Workshop**

  The purpose of this public workshop is to provide an overview of the status of science and research initiatives for generic drugs and an opportunity for public input on these initiatives. Learn more.

- **May 13, 2024: Natural History Studies and Registries in the Development of Rare Disease Treatments- Workshop**

  The Reagan-Udall Foundation for the FDA, in collaboration with FDA's Rare Diseases Team within the Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine; Office of New Drugs; Center for Drug Evaluation and Research and the National Institutes of Health's Division of Rare Diseases Research Innovation within the National Center for Advancing Translational Sciences are hosting a public workshop. This workshop will bring together rare disease patient advocates, academic researchers, regulated industry, and other key stakeholders to discuss considerations for the use of natural history study and registry data in rare disease drug development programs. Learn more.

CAREER OPPORTUNITIES

You want to make a difference.

FDA wants to hire You.

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.

Employment Opportunities

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!