CENTER FOR DRUG EVALUATION AND RESEARCH

What's New in Regulatory Science

Issue I- 2025

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.

May 1, 2025: FDA releases FY 2024 GDUFA Science and Research Report

The Center for Drug Evaluation and Research has published its Generic Drug User Fee Amendments (GDUFA) Science and Research Report for fiscal year 2024. This annually published report describes research activities that supported the development and assessment of generic drug products. Eight scientific areas were identified as GDUFA Science and Research Priority Initiatives for 2024, and accordingly, the report organizes descriptions of active research projects and outcomes into eight chapters corresponding to the eight priority areas, with a ninth chapter reporting on additional generic drug research. Learn more.

April 10, 2025: FDA Announces Plan to Phase Out Animal Testing Requirement for Monoclonal Antibodies and Other Drugs

The U.S. Food and Drug Administration is seeking to advance public health by replacing animal testing in the development of monoclonal antibody therapies and other drugs with more effective, human-relevant methods. The new approach is designed to improve drug safety and accelerate the evaluation process, while reducing animal experimentation, lowering research and development (R&D) costs, and ultimately, drug prices. The FDA's animal testing requirement will be reduced, refined, or potentially replaced using a range of approaches, including AI-based computational models of toxicity and cell lines and organoid toxicity testing in a laboratory setting (so-called New Approach Methodologies or NAMs data). Implementation of the regimen will begin immediately for investigational new drug (IND) applications, where inclusion of NAMs data is encouraged. Learn more.

March 27, 2025: Considerations Rare Disease Drug Development

FDA's Learning and Education to ADvance and Empower Rare Disease Drug Developers initiative published two new videos titled "Understanding the Importance of Endpoints in Rare Disease Drug Development" and "Considerations for Collecting and Using Natural History Study Data that are Fit for Use in the Regulatory Setting" to our educational video series. The videos provide an overview of important considerations for selecting endpoints when designing clinical trials, and concepts to consider when determining how to leverage natural history study data to support regulatory decision making on a marketing application.

March 13, 2025: Case Studies for Rare Disease Drug Development

CDER published two case studies and a case study user guide, developed as part of the Accelerating Rare disease Cures (ARC) Program's Learning and Education to Advance and Empower Rare Disease Drug Developers (LEADER 3D) initiative. These case studies provide examples of approaches successfully used by sponsors when designing and conducting rare disease drug development programs. The ARC Program launched LEADER 3D to better understand and address the unique challenges in bringing rare disease products to market. As part of the initiative, CDER's Rare Diseases Team worked with an independent contractor to conduct interviews with the rare disease drug development community and performed a review of public docket comments to identify educational opportunities across regulatory topics of interest in rare disease drug development. These case studies and the other materials on the LEADER 3D website are reflective of the needs and priorities heard from our valuable partners in the rare disease drug development community. Read the case studies at the LEADER 3D website.

SPOTLIGHT ON CDER SCIENCE

Determining recommended acceptable intake limits of N-nitrosamine impurities, the Carcinogenic Potency Categorization Approach

In collaboration with a consortium of international drug regulatory authorities (the Nitrosamine International Technical Working Group), FDA has developed an approach for predicting the carcinogenicity of N-nitrosamine impurities based on the relative activating and deactivating effects of multiple features in nitrosamines. Easy to use and rapidly applied without the need for specialized software, the Carcinogenic Potency Categorization Approach (CPCA) draws on a larger body of carcinogenicity data than simply determining an acceptable intake (AI) limit based on a single comparator, and it allows an AI limit to be determined when no safety data for the impurity are available. Since it relies only on chemical structure, the new approach can be applied to both known and hypothetical nitrosamine impurities, and it offers applicants and manufacturers a path forward that does not require generating compound-specific data using toxicology studies, which had been a significant limitation. Learn more.

IN PRESS

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

Microphysiological Systems as Drug Development Tools

Opportunities and challenges for human microphysiological systems in drug development

In this review, CDER scientists explore the potential applications of human liver, gut, lung, and cardiac microphysiological systems in drug development with focus on disease modeling, safety assessment, and pharmacokinetic studies. They discuss technical parameters and relevant endpoints for assessing these systems along with challenges such as cell sourcing, reproducibility, and the integration of multiple tissues or organs in a microphysiological system.

Human induced pluripotent stem cell-derived cardiomyocytes and their use in a cardiac organ-on-a-chip to assay electrophysiology, calcium and contractility

Cardiac organs-on-a-chip (Ooc) have the potential to predict cardiac effects of new drug candidates, including unanticipated cardiac outcomes, which are among the main causes for drug attrition. To address concerns about reproducibility, CDER scientists developed a protocol for preparing a cardiac OoC containing cardiomyocytes derived from human stem cells and using them to quantify parameters of cellular electrophysiology, calcium transients, and contractility.

Unraveling Caco-2 cells through functional and transcriptomic assessments

A CDER study of the properties of monolayers composed of caco-2 cells serves as a comprehensive benchmark for evaluating and refining in vitro gut models to enhance their applicability in preclinical testing. The results support the need for advanced in vitro models that can more accurately reflect human intestinal biology.

A 3D Model of the Human Lung Airway for Evaluating Permeability of Inhaled Drugs

CDER investigators report on their assessment an in vitro 3D human lung airway model composed of co-cultured primary human lung epithelial and endothelial cells for predicting the absorption of inhaled drugs.

Addressing the problem of confounding in observational studies of health outcomes

In these two papers, CDER researchers report on simulations-based methods that offers insights for investigators about how to best control for confounding variables and assess the impact of unmeasured confounding in observational studies.

Targeted learning with an undersmoothed LASSO propensity score model for large-scale covariate adjustment in health-care database studies

A simulation-based bias analysis to assess the impact of unmeasured confounding when designing nonrandomized database studies.

Improving our understanding of abuse-deterrent opioid products

Nasal absorption of oxycodone predicted using a novel computational fluid dynamics-physiologically based pharmacokinetic model

CDER researchers report on the influence of particle size and formulation type on exposure to abuse-deterrent oxycodone extended-release drug tablets that are crushed and nasally insufflated. The results were based on a novel modeling approach that combined computational fluid dynamics modeling, a physiologically based pharmacokinetic model, and in vitro dissolution data.

Advanced computational models for continuous manufacturing

Development of a high-fidelity digital twin using the discrete element method for a continuous direct compression process. Part 1. Calibration workflow.

Development of a high-fidelity digital twin using the discrete element method for a continuous direct compression process. Part 2. Validation of calibration workflow.

In these two papers, researchers report on a high-fidelity model based on individual particles of a continuous powder mixer used in drug tablet production that can be used to predict how fluctuations in drug substance concentration at the beginning of the process impact the quality of the final tablets. They discuss the potential of such models to improve development efficiency and quality control in continuous manufacturing.

Narrow Therapeutic Index Drugs: FDA Experience, Views, and Operations

This report summarizes the process at FDA to evaluate candidate narrow therapeutic index (NTI) drugs, provides the current list of NTI drug products for which FDA has published product-specific draft guidance, and outlines FDA's current bioequivalence recommendations for these products.

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 Conversations
Discussions with key Center for Drug Evaluation and Research (CDER) leadership about important regulatory and policy issues.

CDER SBIA Chronicles

FDA/CDER SBIA Chronicles, newsletter of the CDER Small Business and Industry Assistance team, provides industry with useful information to assist in aspects of drug development, marketing and regulation.

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

July 11, 2025: Public Meeting on the Reauthorization of Generic Drug User Fee Amendments (GDUFA)

The Food and Drug Administration (FDA or Agency) is announcing a public meeting to discuss proposed recommendations for the reauthorization of the Generic Drug User Fee Amendments (GDUFA) for fiscal years (FYs) 2028 through 2032. The hybrid public meeting will be held on July 11, 2025, from 9 a.m. to 2 p.m. ET. Learn more.

July 14, 2025, Public Meeting on the Reauthorization of the Prescription Drug User Fee Act (PDUFA)

The Food and Drug Administration (FDA or Agency) is announcing a public meeting to discuss proposed recommendations for the reauthorization of the Prescription Drug User Fee Act (PDUFA) for fiscal years (FYs) 2028 through 2032. The public meeting will be held on July 14, 2025, from 9 a.m. to 2 p.m. Learn more.