CENTER FOR DRUG EVALUATION AND RESEARCH

What's New in Regulatory Science

Issue II- 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.

Unlocking Doors to Better Health. Annual Report

CDER's Office of Clinical Pharmacology (OCP) in the Office of Translational Sciences has published its 2024 Annual Report, entitled "Unlocking Doors to Better Health." Featured in this report is the newly established CDER Quantitative Medicine Center of Excellence, an alliance of several CDER Offices dedicated to maximizing synergies in innovative methods and technologies to advance drug development and improve public health. The report also highlights how OCP has continued to advance regulatory science in support of regulatory review, policy development, research, and public engagement. Download the report.

CDER Scientists Partner with Industry to Develop Critical Reference Materials for Antibody-Drug Conjugates Evaluation

One of the most rapidly growing class of therapeutics, antibody-drug conjugates (ADCs) combine antibody targeting specificity with potent cytotoxic payloads. Under a new Research Collaboration Agreement, scientists at CDER's Office of Pharmaceutical Quality (OPQ) and Sutro Biopharma, Inc., will seek to develop improved analytical standards for ADCs. The research will encompass target antigen selection, payload-linker optimization, and drug conjugation sites that reflect both currently marketed products and those in clinical development pipelines.

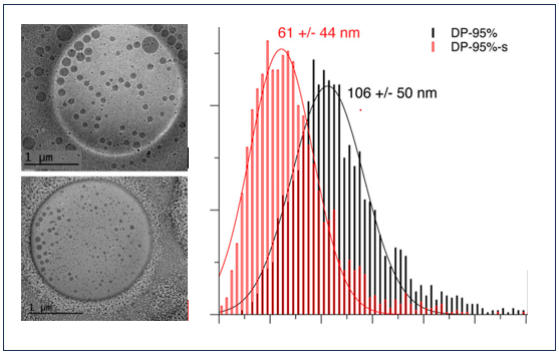
In this collaboration, CDER scientists will:

- Co-lead study design and target selection to ensure regulatory relevance in developing reference materials that meet current and future analytical needs for ADC evaluation
- Apply cutting-edge analytical capabilities to comprehensively characterize ADC reference materials using advanced instrumentation, including mass spectrometry, nuclear magnetic resonance, and functional bioassays
- Generate research outcomes that contribute to broader scientific understanding of ADC characterization methodologies and regulatory best practices

This collaboration enhances OPQ's efforts to strengthen FDA's analytical characterization capabilities for ADCs, directly supporting the FDA's mission to ensure safety, efficacy, and quality of complex biopharmaceuticals. Research results will be made publicly available upon completion.

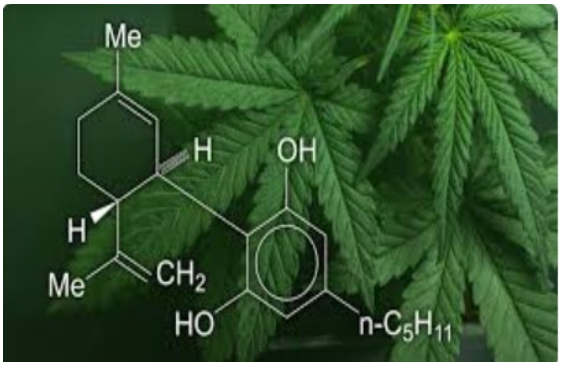
Regulatory Science Impact Stories

A Modern Intact NMR Approach for Characterizing Nanoemulsions



Oil-in-water nanoemulsions are stabilized suspensions of nano-sized drops of oil that by encapsulating poorly soluble drugs improve their solubility and absorption. The performance and stability of these drug delivery vehicles are sensitive to process and formulation parameters that must be carefully controlled to maintain desired drug properties. Due to the lack of non-invasive methods to characterize drug distribution in these emulsions, there are gaps in our understanding of how formulation and process parameters affect the final product, and this has hindered FDA's ability to grant generic drug approvals. To address these gaps, CDER researchers have recently developed nuclear magnetic resonance (NMR) methods that eliminate the need for dilution when characterizing nanoemulsions. Based on data obtained in this study, intact NMR methods for characterization of nanoemulsions can now be recommended to generic drug sponsors. These sensitive and accurate analytical methods have the potential to save resources for the pharmaceutical industry, accelerate generic drug development, and enhance the quality assessment of these drugs, ultimately resulting in lower costs to the American public. Learn more.

CDER investigators address the safety of Cannabidiol in a randomized trial

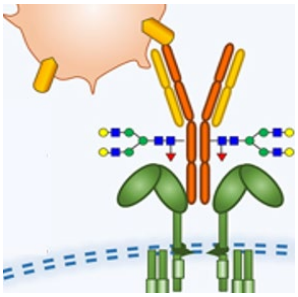


Cannabidiol (CBD) is a nonpsychoactive cannabinoid that is present at relatively high levels in hemp, which is cannabis and derivatives of cannabis with extremely low concentrations of delta-9 tetrahydrocannabinol. In recent years, many unregulated hemp-derived cannabinoid products that contain CBD have become widely available to consumers, raising various safety concerns. A clinical trial conducted by CDER provides rigorous human safety data for cannabidiol at consumer-reported doses consistent with unregulated consumer products. By demonstrating that CBD use, at doses representative of those commonly reported by consumers of unregulated consumer products, can lead to liver enzyme elevations in healthy adults who are not taking any other medications, this study provides evidence that can be used to assess the safety of CBD products and inform discussions about appropriate safeguards. Learn more. Learn more.

IN PRESS

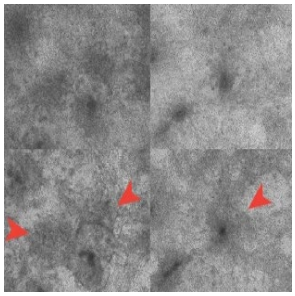
This section provides highlights of select CDER research recently published in scientific journals.

Fc gamma receptor polymorphisms in antibody therapy: implications for bioassay development to enhance product quality



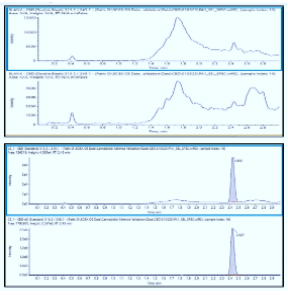
CDER scientists summarize current knowledge of mechanisms through which therapeutic antibodies mediate cell death and how polymorphisms in the receptors on immune cells that recognize the antibody's Fc domain influence these mechanisms. The authors propose approaches through which the drug development community can devise bioassays to assess critical quality attributes of antibody therapeutics while taking the genetic heterogeneity of patients into account.

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



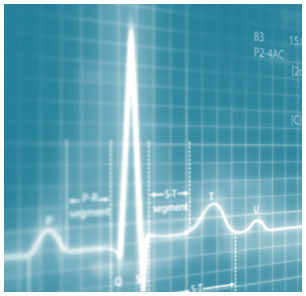
Cardiac organs-on-chips that are made using human induced pluripotent stem cells have the potential to predict cardiac effects of new drug candidates. To promote broad adoption of these tools in drug development and ensure reproducibility, CDER researchers and collaborators have developed a protocol describing how to prepare and use these tools.

Development and validation of a high-throughput LC-MS/MS bioanalytical method for the simultaneous quantification of cannabidiol and metabolites in human plasma



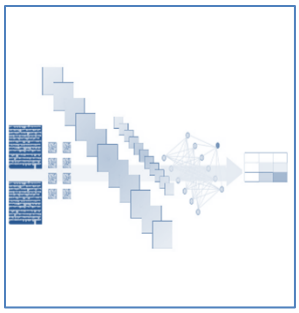
This report describes the development and validation by CDER researchers of a rapid high-throughput bioanalytical method based on liquid chromatography and mass spectroscopy for the quantification of cannabidiol and its primary metabolites in human plasma.

Collaborative science in action: A 20-year perspective from the Health and Environmental Sciences Institute (HESI) Cardiac Safety Committee.



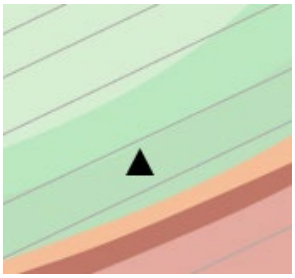
By examining past successes and prospects of the Cardiac Safety Technical Committee of the Health and Environmental Sciences Institute, CDER authors and collaborators shed light on how a multifaceted approach has 1) addressed current challenges in detecting potential cardiac failure modes and 2) paved the way for enhanced drug development and study design methodologies. These methodologies include a focus on improving the translational predictability of nonclinical evaluations and reducing reliance on animal research in cardiovascular safety assessments.

Public feedback to FDA on regulatory considerations for AI in drug manufacturing



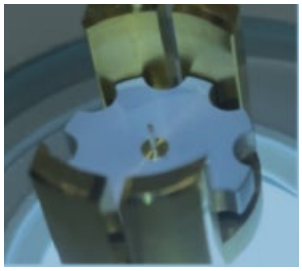
The authors summarize public feedback at a recent workshop where participants were asked to comment on the Agency's recent discussion paper *Artificial Intelligence in Drug Manufacturing*. The input of participants in areas such as data management, governance, model development and validation requirements, and AI in the pharmaceutical quality system are summarized, along with other major concerns of the attendees.

A Tipping Point Method to Evaluate Sensitivity to Potential Violations in Missing Data Assumptions



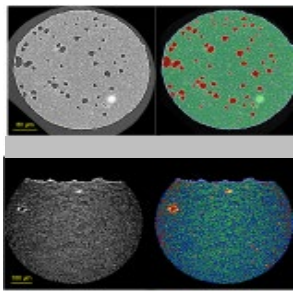
CDER-led research highlights the role of tipping point analyses in the evaluation of the impact of missing data in key analysis results. The authors present a tipping point analysis method that is novel in that it requires no missing data imputation and makes minimal distributional assumptions. The authors showcase the method's use in two real CDER drug reviews.

Quantitative Solid-State NMR Spectroscopy (qSSNMR) in Pharmaceutical Analysis



This mini-review highlights the evolution of quantitative solid-state NMR (qSSNMR), focusing on improvements in detection limits, resolution, and high-throughput capabilities. Technical advancements and applications for analyzing complex pharmaceutical mixtures, and challenges to, and strategies for, widespread adoption are also explored.

Impact of polymer source variations on hydrogel structure and product performance in dexamethasone-loaded ophthalmic inserts



This study established a comprehensive framework of measurement methods to characterize polyethylene glycol-based ophthalmic inserts, using raw materials from multiple vendors as proof of concept. In addition, a preliminary in vitro release testing method was developed to explore how material attributes affect performance of these products.

Upcoming Events

December 5, 2025: Pediatric Developmental Safety Assessment: New Approach Methods

This meeting comes at a critical time for pediatric drug development. An accumulation of knowledge from pediatric drug development programs over the past 25 years provides information that should be used to improve the efficient development of safe and effective new drugs for children. At the same time, the reliance on juvenile animal testing for all pediatric preclinical assessments has run into both the realization of the limitations to this assessment plus the need to develop new approach methods (NAMs) to animal testing as expressed by the U.S. FDA and multiple federal agencies (see FDA-NIH Workshop on Reducing Animal Testing).

In addition, the recent ICH E11A Guidance on Pediatric Extrapolation has indicated that, under some conditions, safety can be extrapolated from the adult population to the pediatric patient population.

Since developmental drug toxicity is not evaluable in the adult population, additional methods must be identified that can answer the critical developmental safety questions raised in the ICH E11A guidance.

Therefore, the goal of this workshop is to discuss new approach methods that can address pediatric developmental safety during drug development. Learn more.

Links to Information about FDA's Regulatory Science Research

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.

FDA: Overview of our Role Regulating and Approving Drugs | Video Series
FDA oversees prescription, generic, biosimilars, and over-the-counter drugs. Learn more.

CDER 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.

CDER 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.

CDER SBIA Chronicles
FDA/CDER SBIA Chronicles, which are podcasts produced by the CDER Small Business and Industry Assistance team, provides industry with useful information to assist in aspects of drug development, marketing, and regulation. Learn more.

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