Generic Drug Science & Research Priorities for Fiscal Year (FY) 2023

Sam Raney, PhD
Associate Director for Science
Office of Research and Standards
Office of Generic Drugs

Generic Drug User Fee Amendments (GDUFA) Science and Research Program

- The FDA funds research proposals received via the **Broad Agency Announcement (BAA) for Advanced Research and Development of Regulatory Science** (*See **Area I.C.4** for research related to generic drugs*)

  https://sam.gov/opp/52766923970840219c29d0ba2f0f4711/view

- The FDA funds research related to generic drugs and bioequivalence (BE) aligned with **GDUFA Science and Research Priority Initiatives** for each FY

  https://www.fda.gov/drugs/generic-drugs/science-research

GDUFA Science and Research Priority Initiatives for FY 2023

- Develop Methods for Generics to Address Impurities such as Nitrosamines
- Enhance the Efficiency of BE Approaches for Complex Active Ingredients
- Enhance the Efficiency of BE Approaches for Complex Dosage Forms and Formulations
- Enhance the Efficiency of BE Approaches for Complex Routes of Delivery
- Enhance the Efficiency of BE Approaches for Complex Drug-Device Combination Products
- Improve the Efficiency of BE Approaches for Oral and Parenteral Generic Products
- Facilitate the Utility of Model-Integrated Evidence (MIE) to Support Demonstrations of BE
- Expand the Use of Artificial Intelligence (AI) and Machine Learning (ML) Tools

Develop Methods for Generics to Address Impurities such as Nitrosamines

A. Evaluating practical strategies that may mitigate the potential risks of harmful impurities such as nitrosamine adducts without impacting the BE or quality of a generic product

B. Developing analytical methods, and approaches using orthogonal methods, for the identification and quantitation of nitrosating species in ingredients, including considerations for the distribution of nitrosating species in an ingredient or drug product

C. Characterizing the reactivity of different amines (e.g., secondary vs. tertiary amines) to support risk assessments that consider the potential for endogenous nitrosation

Develop Methods for Generics to Address Impurities such as Nitrosamines

D. Improving in vitro, in silico or in vivo (animal) models to predict the risk of differences in impurities between a prospective generic product and its reference listed drug

E. Estimating acceptable intake amounts for impurities such as nitrosamine adducts (e.g., nitrosamine drug substance related impurities; NDSRIs) using certain mutagenicity evaluations or quantitative structure activity relationship modeling

Enhance the Efficiency of BE Approaches for Complex Active Ingredients

A. Improving methods for characterizing the sameness of peptide or oligonucleotide active ingredients and the formation of associated impurities

B. Improving methods for assessing the immunogenicity of peptide or oligonucleotide products and associated impurities

Enhance the Efficiency of BE Approaches for Complex Dosage Forms and Formulations

A. Elucidating drug release mechanisms, critical quality attributes (CQAs), and characterization test methods for long-acting injectable, insertable or implantable (collectively, LAI) products with the goal of predicting in vivo performance

B. Improving characterization tools for polymeric ingredients and related complex formulations to support assessments of qualitative sameness

Enhance the Efficiency of BE Approaches for Complex Routes of Delivery

A. Implementing characterization-based (in vitro) methods, potentially together with in vivo PK and modeling methods, as alternatives to the use of comparative clinical endpoint BE studies for nasal and inhaled drug products

B. Developing efficient BE methods for topical drug products (applied to skin or other areas for local action) that may contain compositional differences relative to the reference standard

C. Improving comparative in vitro permeation test (IVPT) and in vivo cutaneous pharmacokinetics (PK)-based study designs and data analysis techniques that help to resolve practical challenges with implementing these methodologies to support a demonstration of BE for topical drug products

Enhance the Efficiency of BE Approaches for Complex Drug-Device Combination Products

A. Improving data analysis approaches for assessing comparative task analysis and comparative use human factors study results

B. Developing improved criteria for comparative device performance assessments that would support a demonstration of BE by in vitro methods (e.g., predictive adhesion performance of transdermal delivery systems) to eliminate the need for certain in vivo studies

C. Developing efficient approaches to support transitions by generic products to utilize more environmentally friendly propellants

Improve the Efficiency of BE Approaches for Oral and Parenteral Generic Products

A. Utilizing physiologically-based PK (PBPK) modeling to identify risk factors for food effects and formulation dependent drug interactions for orally-administered products to support global harmonization of the most efficient BE approaches for these products

B. Elucidating how ingredients commonly used to modify drug release in orally-administered modified release (MR) products function, to facilitate the implementation of risk-based approaches to support biowaivers for MR products, and to elucidate BE considerations for special patient populations

Improve the Efficiency of BE Approaches for Oral and Parenteral Generic Products

C. Developing evidence to support the feasibility of efficient BE methods for parenteral drug products that may contain compositional differences relative to the reference listed drug, and to support global harmonization of the most efficient BE approaches for these products

Facilitate the Utility of Model-Integrated Evidence (MIE) to Support Demonstrations of BE

A. Advancing complementary approaches using MIE to support a demonstration of BE specifically for inhalation and topical routes of delivery as well as for LAI products

B. Establishing best practices for model standardization, validation, acceptance, and sharing (e.g., using model master files) that improve the reproducibility and reusability of quantitative pharmacology information used in BE study simulations

Expand the Use of Artificial Intelligence (AI) and Machine Learning (ML) Tools

A. Improving the use of real-world evidence for post-market surveillance of generic drug substitution and for evaluating the impact of generic drugs on public health

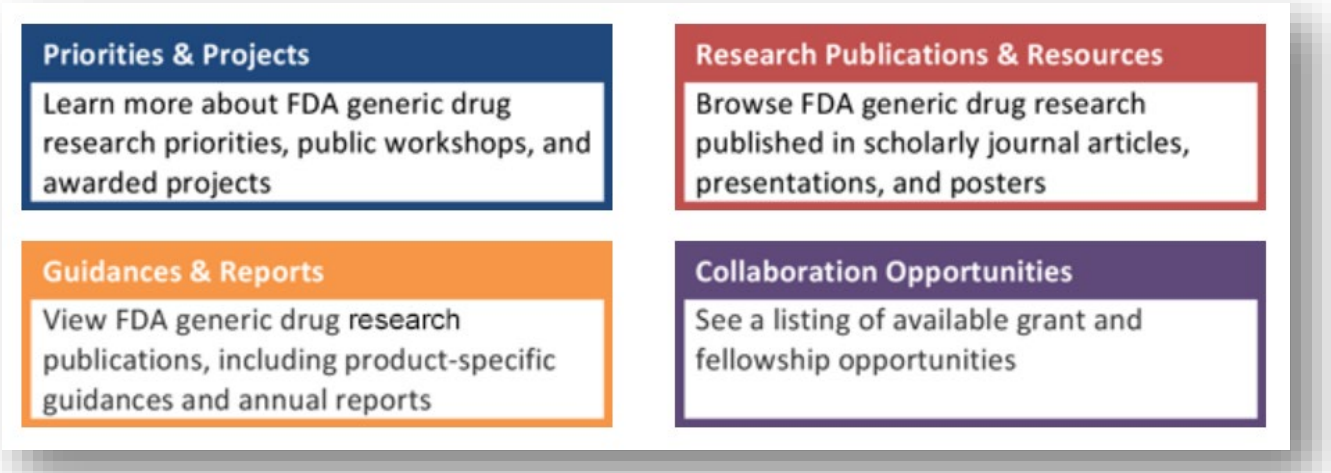
B. Integrating AI/ML tools with information and data available to FDA, and identifying strategies to optimize the reliability of outcomes produced by these tools

C. Exploring the capability of AI/ML tools for a prospective applicant to be able to efficiently assess the completeness of its ANDA prior to submission, and to enhance the efficiency, consistency, and quality of regulatory assessments once ANDAs are submitted

Generic Drug User Fee Amendments (GDUFA) Science and Research Program

- Learn more about generic drug science and research collaboration opportunities on FDA's website:

https://www.fda.gov/drugs/generic-drugs/science-research




FDA
U.S. FOOD & DRUG
ADMINISTRATION