Generic Drug Science & Research Priorities for FY 2024

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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, and evaluating the effect of these strategies on the absorption and/or the bioavailability of active pharmaceutical ingredients (APIs), including utilizing modeling and simulation approaches to assess the risk of altering the performance of a generic product in the event of a reformulation

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

Develop Methods for Generics to Address Impurities such as Nitrosamines

C. Elucidating the reactivity of different functional groups in APIs (e.g., tertiary amines beyond secondary amines) or other factors that may improve the ability to predict formation of nitrosamine drug substance related impurities (NDSRIs) or small molecule nitrosamines and the risks of their formation under relevant conditions for pharmaceuticals

D. Estimating acceptable intake amounts for impurities such as nitrosamine adducts (e.g., NDSRIs) using certain mutagenicity evaluations (involving in vitro, in silico or in vivo (animal) models) or using quantitative structure activity relationship modeling

Enhance the Efficiency of BE* Approaches for Complex Active Ingredients

A. Developing novel analytical methods, as well as improving and standardizing existing methods, to characterize components (including impurities) that can support a demonstration of sameness for oligonucleotide APIs

B. Improving and standardizing in vitro methods for assessing the immunogenicity of peptide or oligonucleotide products, including associated impurities

*BE = bioequivalence

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

A. Elucidating drug release mechanisms, critical quality attributes, 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 pharmacokinetics (PK) and modeling methods, as alternatives to 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 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 or anthropometric evaluation of device design changes for injectable and inhaled drug products) 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 oral physiologically-based PK (PBPK) modeling to identify risk factors for food effects and formulation dependent drug interactions (e.g., proton pump inhibitors) 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 and ophthalmic 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 an efficient demonstration of BE specifically for locally-acting products (e.g., 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 FDA information and data to support quantitative analyses and modeling approaches that facilitate regulatory assessments, and identifying strategies to optimize the reliability of outcomes produced

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


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