FY 2016 Awarded GDUFA Regulatory Research Contracts and Grants

Evaluation of formulation dependence of drug interaction with proton pump inhibitors (PPIs)

- Awarded to Biopharma Services USA Inc. (#HHSF223201610004I/HHSF22301001T)
- The project aims to evaluate whether co-administration with PPIs/antacids will impact the bioequivalence of oral modified release products. PPIs/antacids are known to elevate gastric pH and potentially affect in vivo drug release, but there is minimal data on whether these effects are significant enough to impact conclusions of bioequivalence. The study results will help the Agency gain a better understanding of drug-drug interaction between oral modified release products and PPIs/antacids and establish bioequivalence standards for generic oral extended release products.

Pulsatile microdialysis for in vitro release of ophthalmic emulsions

- Awarded to Physical Pharmaceutica LLC (#HHSF223201610105C)
- This project aims to develop an in vitro drug release testing method using pulsatile microdialysis and to evaluate its application for ophthalmic emulsions.
- The accomplishment of this project is expected not only to report a sensitive drug release method for ophthalmic emulsion products but also to understand the drug release mechanism and the critical parameters that may affect the release profile from emulsion formulations. This will help in the review of Abbreviated New Drug Applications (ANDAs) and in the development of guidance documents for emulsion products.

Critical process parameters for the preparation of Amphotericin B liposomes

- Awarded to Neo-Advent Technologies LLC (#HHSF223201610093C)
- This project aims to test how the critical physicochemical attributes of liposomal amphotericin B can be affected by differences in these manufacturing processes as well as develop and verify analytical methods to test product bioequivalence.
- This research project will strengthen the FDA's knowledge when advising stakeholders and ANDA sponsors of liposomal products as well as ensure that the Agency is aware of potential manufacturing and analytical issues when assessing product bioequivalence for complex liposomal formulations.

Pharmacokinetic comparison of locally acting orally inhaled drug products

- Awarded to University of Florida (#HHSF223201610099C)
- The objective of this project is to evaluate whether pharmacokinetic profiles are sensitive to dry powder inhaler (DPI) formulations that differ in the central to peripheral (C/P) lung deposition ratio. A clinical study will be conducted to evaluate the pharmacokinetic profiles of healthy adult subjects after a single-dose of different orally inhaled formulations is administered using a DPI.
- The study results will impact FDA's regulatory decision making for generic inhalation products as they contribute to the bioequivalence review process and provide scientific information for the development of new (and revisions or existing) bioequivalence guidance documents.

Advanced analytical techniques for mixed polymer drug-delivery systems

- Awarded to Akina, Inc. (#HHSF223201610091C)

- The objective of this project is to provide scientific guidance on how to identify and distinguish different types of Poly(lactide-co-glycolide) (PLGA) polymers when used as a mixture in a drug product. The goal of this project is to develop an assay protocol that can be used to determine two different types of PLGA polymers in a blend based on their lactide (L) to glycolide (G) ratios.
- The outcome of this project will be helpful for both the pharmaceutical industries and the Agency to develop and approve generic long-acting injectable products using PLGA polymers which are required to be qualitatively and quantitatively the same as the reference product.

Mass spectrometry profiling of pentosan polysulfate in urine

- Awarded to Battelle Memorial Institute (#HHSF223201610114C)
- The objective of this project is to explore and develop an IMS-MS based method to profile pentosan polysulfate sodium (PPS) in urine with the ultimate goal of developing a sensitive, accurate and reproducible bioanalytical tool. This project aims to identify appropriate methods to extract PPS from urine and then employ IMS-MS to characterize PPS samples for profiling.
- The study results will contribute towards development of a tool which may be used to establish bioanalytical guidelines for determining bioequivalence of PPS.

Assessment of the in vitro percutaneous absorption, in vitro rate of release, and physicochemical properties of selected commercially available AT rated ointment formulations

- Awarded to QPS, LLC (#HHSF223201610125C)
- This first objective of this project aims to compare the topical bioavailability of active ingredients from commercially available AT-rated ointments with that from their respective reference listed drug products using an in vitro permeation test. The second objective is to compare the physicochemical product quality (Q3) and performance (in vitro release test) attributes between the AT-rated ointments with their reference listed drug products.
- The outcomes of this project are intended to support the development of new, evidence-based standards for bioequivalence and therapeutic equivalence of generic drug products, particularly for locally acting topical ointment drug products.

Evaluation of model-based bioequivalence statistical approaches for sparse design pharmacokinetic studies

- Awarded to University of Paris (#HHSF223201610110C)
- This project aims to develop, evaluate and compare model-based methods to analyze bioequivalence studies with sparse pharmacokinetic designs with the aim to find adequate statistical approaches to control type I errors and to achieve sufficient power to conclude bioequivalence using nonlinear mixed-effects models.
- The study results will help facilitate the drug development and regulatory review of products that can only be tested in bioequivalence studies with sparse pharmacokinetic designs.

Investigation of peptide-PLGA interactions in microsphere drug products

- Awarded to University of Michigan (U01FD005847)
- The purpose of this project is to develop a systematic approach to fully characterize peptide-polymer interactions in PLGA based microsphere dosage forms. The developed approach will be able to identify the different types of peptide-polymer interactions, quantify the isolated peptide impurities, and determine the formulation parameters, dosage form dynamics, and manufacturing processes responsible for facilitating peptide-polymer interactions.

- The study results will provide better understanding of peptide-polymer interaction in PLGA based drug delivery systems, which will help the FDA develop guidances for generic microspheres containing peptide drugs.

Implementing population pharmacokinetic modeling algorithm in physiologically based pharmacokinetic (PBPK) models to allow parameter estimation at individual data level

- Awarded to Colorado State University (U01FD005838)
- The purpose of this project is to develop and implement a robust optimization algorithm that can be used to perform population-based statistical analysis in complex and computationally intensive PBPK models so that knowledge of parameter distributions in the population(s) of interest can be better informed.
- The developed models may be applied to generate improved predictions on the drug absorption and disposition from generic drug products to support generic drug development and regulatory reviews.

Assessment of intersubject variability of small airway delivery with oral inhalation drug products

- Awarded to University of Iowa (U01FD005837)
- This objective of this project is to characterize drug delivery to the small airways in adult asthmatic patients using a computational modeling approach. The approach will consider the effects of intersubject variability, especially as it relates to differences in lung morphology, inhalation pattern, and airway constriction.
- The outcome of the study will be a population estimate that may be used to categorize drug products based on whether or not a significant effect on small airway constriction may be expected. Improved prediction of inhalation drug delivery will help FDA revise or optimize bioequivalence recommendations for this product category.

Generic Drug Substitution in Special Populations

- Awarded to Auburn University (U01FD005875)
- The purpose of this study is to: 1) collect information on generic substitution to assess therapeutic interchangeability between brand name and generic products in special patient populations ; 2) compare clinical practice patterns with labeled drug administration information in the assessed populations; and 3) analyze the impact of product-level, patient-level, and provider-level factors on generic drug substitution.
- The outcome of this study will help identify research needs, support FDA's regulatory science efforts to monitor and ensure successful generic substitution, and provide evidence to assure the public on generic drug safety and effectiveness.

Bioequivalence of topical products: comparing dermal pharmacokinetics by microdialysis or microperfusion techniques

- Awarded to Joanneum Research (U01FD005861) and Long Island University (U01FD005862)
- The continuous in vivo measurement of drug concentrations in the dermis by either dermal open flow microperfusion (dOFM) or dermal microdialysis (dMD) can theoretically be used to compare the bioavailability of a topically administered drug from test and reference products. Joanneum Research will use dOFM to assess the pharmacokinetics of topically applied drug products. Long Island University will use dMD to assess the pharmacokinetics of topically applied drug products.

- The study results will help support the development of an accurate, sensitive and reproducible methodology to monitor and compare the dermal pharmacokinetics of topically administered drugs.

Integrating supersaturation-precipitation mechanisms in mechanistic oral absorption models for predicting in vivo performance

- Awarded to Simcyp Limited (1U01FD005865)
- The objectives of the study are to: 1) develop and establish a comprehensive mechanism-based absorption model to predict in vivo PK profiles of supersaturating formulations, and 2) to further establish an IVIVC for each of these drug products.
- The developed model will be used to gain mechanistic insights on the in vivo performance of oral supersaturating drug delivery systems.

Stable isotope dilution ultrafiltration method to evaluate bioequivalence of nanomedicines

- Awarded to National Cancer Institute (224-16-30015)
- This project aims to utilize a novel stable isotope dilution method for quantification of nanomedicines present as encapsulated and unencapsulated fractions.
- The results from this project will contribute to the development of a novel method for evaluation of bioequivalence for generic nanoproducts.