FY 2013 Awarded GDUFA Regulatory Research Contracts and Grants

Development of In Vivo Predictive Dissolution Method for Orally Inhaled Drug Products

- Multiple Awards to: University of Bath (1 U01 FD004953-01), University of Florida (1 U01 FD004950-01), Virginia Commonwealth University (1 U01FD004941-01)
- The goal of these grants is to develop an in vitro dissolution method for orally inhaled drug products (OIDPs) which will be capable of predicting in vivo dissolution of drugs that are administered via the inhalation route. The outcome of the project will aid in development of a tool that could be used for formulation development and optimization as well as product quality control. The multiple awards allow the evaluation of alternative approaches.

Systematic Evaluation of Excipient Effects on the Efficacy of Metered Dose Inhaler Products

- Awarded to Cirrus Pharmaceuticals, Inc (1 U01 FD004943-01)
- The goal of this grant is to investigate the effect of excipient concentrations on the aerosolization performance of typical hydroflouroalkane (HFA) - based metered dose inhaler (MDI) formulations, as well as to evaluate the sensitivity of in vitro methods in detecting excipient concentration changes. Success would support allowing differences in inactive ingredients in generic MDI products.

Investigate the Sensitivity of Pharmacokinetics in Detecting Differences in Physicochemical Properties of the Active in Suspension Nasal Products for Local Action

- Awarded to University of Florida (HHSF223201310220C)
- The contract will investigate the effect of physicochemical properties of the active in suspension nasal drug product for local action including, but not limited to, particle size, morphic form and solvation state on the pharmacokinetic behavior of the drug product. This project could lead to a new bioequivalence approached for nasal spray suspension products.

Effect of Different Protective Packaging Configurations on Stability of Fluticasone Propionate Capsules for Inhalation

- Awarded to University of Florida (HHSF223201300479A)
- This contract will comprise packaging of the fluticasone propionate capsules using different packaging materials to determine the optimum packaging that will ensure stability of this drug product during shipping and the intended period of use in a research study. This contract supports previous awarded research activities on inhalation bioequivalence.

In Vitro Release Tests for Transdermal Drug Delivery Systems

- Multiple Awards to University of Cincinnati(1 U01FD004942-01) and University of Maryland (1 U01 FD004955-01)
- These grants will investigate in vitro - in vivo correlations of transdermal systems. The goal is to identify in vitro release test conditions that best identify heat effects on transdermal system release. The University of Maryland award will include in vivo studies while the University of Cincinnati will focus on modeling of heat effects.

In Vitro Release Tests for Topical Dermatological Products

- Awarded to Joanneum Research (1U01 FD004946-01) and University of Maryland (1U01FD004947-01)
- These grants investigate in vitro - in vivo correlations of topical dermatological products. The goal is to identity in vitro release test conditions that are best correlated with in vivo performance and thus provide alternative approaches to bioequivalence for topical products. The University of Maryland award is five year award for investigation of multiple methods across a range of products. The Joanneum Research award will support a human Open Flow Microperfusion study to evaluate the potential for this type of in vivo study to support bioequivalence of topical products.

Correlation of Mesalamine Pharmacokinetics with Local Availability

- Awarded to University of Michigan (HHSF223201300460A)
- This contract is to establish quantitative correlation of plasma PK data with local GI concentration and to improve physiologically based models for colon absorption. Results could lead to new approaches to the bioequivalence of locally acting GI drugs and improved understanding of colon absorption from modified release products.

In Vitro and In Vivo Correlations of Ocular Implants

- Awarded to University of Colorado Denver (I 1U01FD004929-01) and Auritec Pharmaceuticals, Inc (1U01FD004927-01)
- The purpose of these grants is to investigate in vitro-in vivo correlations of ophthalmic intravitreal implants. In each award, an in vitro dissolution test which correlates with in vivo ocular absorption will be investigated and compared to an animal model. The two awards will study different drugs and could help develop in vitro bioequivalence methods or improved release tests for this product category.

In vitro-In vivo Correlations of Parenteral Microsphere Drug Products

- Awarded to University of Connecticut Storrs (1U01FD004931-1) and University of Michigan (1U01FD005014-1)
- The purpose of these grants is to investigate in vitro-in vivo correlations of parenteral microspheres. An in vitro dissolution test which correlates with in vivo absorption will be investigated. The two awards will study different drugs and could lead to better guidance for industry on the development of in vitro release tests for parenteral microspheres. Better in vitro release tests will also accelerate product development of generic microsphere formulations.

Prediction of In Vivo Performance for Oral Solid Dosage Forms

- Awarded to the University of Michigan (HHSF223201310144C)
- The purpose of this contract is to improve prediction of in vivo performance of oral solid dosage forms. The scope includes modeling of GI fluid hydrodynamics, sampling of GI tract fluids composition and pH, novel dissolution methods and in vivo PK studies to validate model predictions.

Collection of Dose Adjustment and Therapeutic Monitoring Data for Narrow Therapeutic Index (NTI) Drug Classification

- Awarded to Duke University (1U01FD004858-01) and Johns Hopkins University (1U01FD004859-01)
- The objective of this grant is to collect drug dose adjustment and therapeutic monitoring data in patients to aid NTI classification. The two awards will use different medical record databases.

Bioequivalence of Generic Buproprion

- Awarded to Washington University (1U01FD004899-01)
- The purpose of this multi-year grant is to (1) demonstrate bioequivalence between generic and brand name bupropion HCl modified release products with different release patterns at steady state in patients, and (2) evaluate whether patients can perceive the difference in release pattern and experience lack of efficacy or increased adverse events after they are switched between each treatment. This grant (along with the two following awards) is part of broader effort to better understand the root cause of recent problems with bioequivalence of bupropion.

Investigation of Inequivalence of Bupropion Hydrochloride Extended Release Tablets: In Vitro Metabolism Quantification

- Awarded to University of Michigan (HHSF223201310183C)
- The objective of this contract is to conduct detailed in vitro metabolism studies on bupropion that will study the enzymes involved in bupropion metabolism as well as the enzyme kinetics to provide data for further investigation on inequivalence issue of the bupropion HCl extended release product.

Pharmacokinetic Study of Bupropion Hydrochloride Products with Different Release Patterns

- Awarded to University of Michigan (HHSF223201310164C)
- The objectives of this contract are to conduct healthy subject pharmacokinetic studies of bupropion HCl modified release products with different release patterns and different doses. This will help FDA understand how the release pattern of bupropion HCl products and the genotype of metabolic enzyme may affect the bioequivalence conclusions across different dose strengths within one product line due to the saturation of intestinal metabolism.

Evaluation of Drug Product Formulation and In-Vitro Performance Characteristics Related to Abuse-Deterrence for Solid Oral Dosage Forms of Opioids

- Awarded to National Institute for Pharmaceutical Technology and Education (HHSF223201301189P)
- The contract will investigate the effect of physicochemical properties of the active and excipients and composition of the drug product, along with the drug product manufacturing technology on the manipulation of the drug product for extraction of the active ingredient for putative abuse. This investigation will employ various mechanical and chemical manipulation techniques, commonly used by abusers, to assist in extraction of the active from the drug product, coupled with in-vitro characterization techniques. The goal is to have a better understanding of how material properties of excipients impact abuse-deterrent properties. This work will inform future FDA guidance on the evaluation of abuse deterrent formulations in ANDAs.

Postmarketing Surveillance of Generic Drug Usage and Substitution Patterns

- Awarded to Brigham and Women's Hospital (1 U01 FD004856-01) and University of Maryland Baltimore (1 U01 FD004855-01)
- The purpose of these grants are to evaluate existing tools and to develop new methods to proactively monitor the drug safety, efficacy, usage, and substitution patterns of recently approved generic drugs whose approval was controversial and to evaluate if controversy during the approval process affects their acceptance by physicians and patients. The results will help FDA develop surveillance plans for future generic drug approvals

Evaluation of Clinical and Safety Outcomes Associated with Conversion from Brand-Name to Generic Tacrolimus Products in High Risk Transplant Recipients

- Awarded to University of Cincinnati (HHSF223201310224C)
- The objectives of this contract are to monitor the tacrolimus trough concentration in high immunologic risk patient populations after switching of all marketed tacrolimus capsule products and to evaluate the necessity of therapeutic monitoring following each substitution. This study will evaluate clinical and safety outcomes among higher risk transplant recipients whose tacrolimus was converted from the brand-name formulation to multiple generic formulations. Results from this project will support generic substitution in all transplant patients.

Development of Bio-Relevant In-Vitro Assay to Determine Labile Iron in the Parenteral Iron Complex Product

- Awarded to Albany College of Pharmacy (1U01FD004889-01)
- The objective of this grant is to evaluate various in-vitro methods of determining labile iron and develop a bio-relevant in-vitro method to predict the amount of non-transferrin bound iron in vivo. Results from this project will improve in vitro release tests for iron complexes and allow FDA to provide consistent guidance to ANDA sponsors on this topic.

Evaluation of Dissolution Methods for Complex Parenteral Dosage Forms

- Awarded to University of Kentucky (1U01FD004892-01) and ZoneOne Pharma, Inc (1U01FD004893-01)
- The objective of these grants is to evaluate current in vitro release methods for complex parenteral dosage forms and analyze their capability of detecting formulation differences, predicting in-vivo performance, as well as their method robustness. The two awards will study different liposomal formulations. Better in vitro release methods will accelerate product development of generic liposomal formulations.