CENTER FOR RESEARCH ON COMPLEX GENERICS

Advances in PBPK Modeling and its Regulatory Utility for Oral Drug Product Development

Welcome Remarks

James Polli, PhD

October 12, 2023

UNIVERSITY of MARYLAND BALTIMORE

UNIVERSITY OF MICHIGAN

FDA U.S. FOOD & DRUG ADMINISTRATION

Established in 2020, The Center for Research on Complex Generics (CRCG) is a collaboration between the University of Maryland, the University of Michigan, and the FDA.

About CRCG

Our Mission

Increase access to safe and effective generic drugs through enhanced infrastructure/communication, education, and research collaboration across industry, academia and the FDA.

We are dedicated to advancing programs that stimulate scientific dialogue, disseminate current insights, and generate new knowledge about complex generics in support of the FDA's mission to promote and protect the public health.

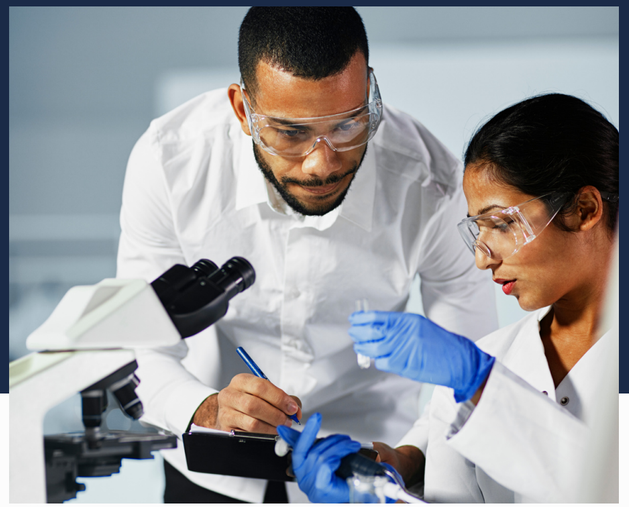
Primary Goals of the CRCG

INFRASTRUCTURE & COMMUNICATION

Establishing core program infrastructure and enhancing communications to advance complex generics development

EDUCATION & TRAINING

Providing education and training through workshops, webinars, hands-on demonstrations, and on-site visits



COLLABORATIVE RESEARCH

Conducting collaborative research and enabling pilot research projects and technological development

Ongoing Engagement to Advance Complex Generics Product Development

300+ engagements with key complex generics players to understand challenges and opportunities in advancing complex generics product development

Challenges and need for modeling and simulation for generic drug development

- FDA acceptance of using more predictive in vitro studies and modeling, rather than human factor studies, would benefit industry sponsors looking to enter into the pediatric field.
- Need for appropriate model-based alternatives to bioequivalence studies to speed up the development process and reduce costs
- Lack of case studies even though the agency is engaged and enthusiastic and are willing to work on the issues faced by industry
- Need for global harmonization in acceptance of modeling approaches for approval of generic drugs across multiple agencies

Modeling and simulation- few applications of interest

- PBPK for inhalation products and solid oral doses
- Population PK for assessing absorption sites
- Fed state gastrointestinal models with extrapolation from fasted patient data
- Partial modeling for limited patient populations to round out small trials
- Product class specific models

10 Educational Workshops & Training Completed

~22,000 Registered

UPCOMING 2023 IN-PERSON (& VIRTUAL) WORKSHOPS & TRAINING

DECEMBER 7-8

Characterization of Complex Excipients/Formulations

SAVE- THE- DATE 2024 In-Person (& Virtual) Workshops & Training

MARCH 14-15

Drug-Device Combination Products: Updates and Challenges in Demonstrating Generic Substitutability

MAY 2

Considerations and Potential Regulatory Applications for a Model Master File

OCTOBER 7-8

Scientific and Regulatory Considerations for Assessment of Immunogenicity Risk for Generic Peptide and Oligonucleotide Drug Products: Present State and Future Directions

NOVEMBER 7

Updates on Approaches to Acceptable Intakes of Nitrosamine Drug Substance Related Impurities (NDSRIs) and Bioequivalence Assessment for Reformulated Drug Products

DECEMBER 4-5

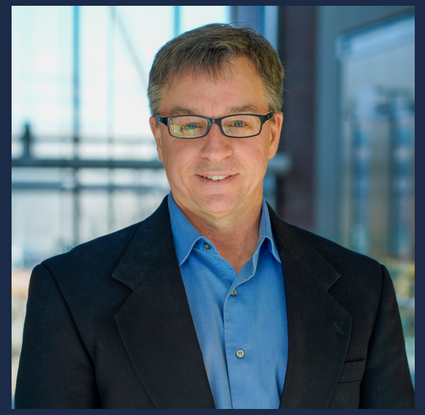
Navigating the Transition to Low Global Warming Potential Propellants

Ongoing Research

2 Research projects completed on model-integrated approaches to demonstrate bioequivalence for long-acting injectable generic products

- Analytical characterization of ONIVYDE™ and irinotecan liposome
- Evaluation of micelle/colloid diffusivity to better parameterized physiologically based pharmacokinetic models for oral drug absorption
- Validation of simulated airway mucus models for predicting bioavailability / local exposure of inhaled drugs and characterization of MDI products, particle size, dissolution, particle morphology
- Characterization of PLGA-peptides products purity and immunogenicity
- Biowaiver consideration for added antioxidants: effect of antioxidants on drug intestinal permeability

CRCG Team



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Learn more about the Center & signup for listserv

www.complexgenerics.org

YouTube Channel

Recordings from CRCG events will be posted here. Subscribe for updates.

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Social Media

Please follow CRCG for event related updates.

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CRCG Fall 2023 Survey: Generic Drug Industry Insights, Challenges and Opportunities

Mid-October 2023

www.complexgenerics.org

Upcoming Survey

Thank You for Your Participation!

Opening Remarks- Powers and Problems in PBPK Models

by
Dr. William Jusko

SUNY Distinguished Professor

University of Buffalo

Overview of Workshop by Dr. Liang Zhao

Director, DQMM, ORS, OGD, FDA