

Fiscal Year (FY) 2023 Generic Drug Science and Research Initiatives Public Workshop

May 11-12, 2023

In-person & Virtual

Agenda (Day 1)

8:00 AM – 8:15 AM **Opening Remarks**
 Robert Lionberger, PhD Director, ORS, OGD, CDER, FDA
 Robert Califf, MD Commissioner of Food and Drugs

8:15 AM – 8:30 AM **Joint Directors' Message on the FY 2023 Generic Drug Science and Research Initiatives Public Workshop**
 Susan Rosencrance, PhD Acting Director, OGD, CDER, FDA
 Michael Kopcha, PhD Director, OPQ, CDER, FDA

Session 1: Oral Products

Sub-Session 1A: Development of Efficient Methods for Generics to Address Impurities Such as Nitrosamines

This session will discuss what research is needed to develop efficient bioequivalence standards for products that are reformulated to mitigate nitrosamine risk, elucidate excipient effects related to nitrosamine impurity formation, address potential concerns related to the mutagenicity or carcinogenicity of reactive impurities in certain drug products, and identify other aspects of emerging issues related to nitrosamines. This session will also discuss what research is needed to facilitate the use of quantitative methods, modeling, simulation, or AI/ML tools to address challenges for generic product development related to impurities such as nitrosamines.

8:30 AM – 8:45 AM **Proposed Methods to Set Limits for Nitrosamine Drug Substance Related Impurities (NDSRIs)**
 Raphael Nudelman, PhD Sr. Director Impurity Expert, R&D, Teva Pharma

8:45 AM – 9:00 AM **Effects of Antioxidants in Drugs Products on Intestinal Drug Transporters**
 Sook Wah Yee, M. Pharm, PhD Assistant Adjunct Prof., University of California, San Francisco

9:00 AM – 9:15 AM **Nitrosamine Additives Mitigation Studies**
 Diaa Shakleya, PhD Principal Investigator, DPQR, OTR, OPQ, CDER, FDA

9:15 AM – 10:00 AM **Panel Discussion**
Co-Moderator: Andre Raw, PhD Associate Director for Science and Communication, OLDP, OPQ, CDER, FDA
Co-Moderator: Liang Zhao, PhD Director, DQMM, ORS, OGD, CDER, FDA

Panelists:

Khondoker Alam, PhD	Senior Pharmacologist, DQMM, ORS, OGD, CDER, FDA
Robert Dorsam, PhD	Director, DPTR, OSCE, OGD, CDER, FDA
Martin Ehlert, PhD	Vice-president, Global API R&D, Apotex
Raphael Nudelman, PhD	Sr. Director Impurity Expert, R&D, Teva Pharma
Diaa Shakleya, PhD	Senior Pharmacologist & Principal Investigator, DPQR, OTR, OPQ, CDER, FDA
Daniel Snider, PhD	Head, Global Quality Systems/QA IT Technical Quality, Viatris
Ethan Stier, PhD	Associate Director, OCP, OTS, CDER, FDA
Sook Wah Yee, PhD	Assistant Adjunct Prof., University of California, San Francisco

10:00 AM – 10:15 AM **Coffee Break**

Sub-Session 1B: Enhancing the Efficiency of Bioequivalence Approaches for Generic Oral Products

This session will discuss what research is needed to develop efficient bioequivalence standards for generic oral products, including orally disintegrating tablets, exploring what research is needed to expand the scope of biowaivers through in vitro testing in lieu of fed-BE studies for IR oral products; integrating in vitro and in silico modeling to support biowaivers; and advancing research on clinically relevant dissolution testing. This session will also discuss what research is needed to support global harmonization (e.g., ICH M13 that intends to harmonize BE standards for IR solid oral dosage forms) across regulatory agencies, as well as research to support strategies for bridging to reference standards (in vitro vs. in vivo PK) and patient vs. subject recruitment for PK BE studies. This session will also discuss what research is needed to facilitate the use of quantitative methods, modeling, simulation, or AI/ML tools to improve the efficiency of BE approaches for generic oral products.

10:15 AM – 10:30 AM **Research Needed to Develop Efficient BE Standards for Orally Disintegrating Tablets**
 Ilan Zalit Sr. Director of Gx R&D, Teva Pharma

10:30 AM – 10:45 AM **Use of a Model-Integrated Approach for an Efficient Demonstration of BE**
 Yu Chung Tsang, PhD Chief Scientific Officer, Biopharmaceutics & Biostatistics, Apotex

10:45 AM – 11:00 AM **Alternate Approaches to In Vivo Bioequivalence for Site Transfer of Modified Release Product**
 Makarand Avachat, M. Pharm Executive Vice-President, Pharmaceutical R&D, Lupin Ltd., India

11:00 AM – 11:15 AM **Regulatory Science to Support Global Harmonization for Establishing BE for Generic Oral Products**
 Lei Zhang, PhD Deputy Director, ORS, OGD, CDER, FDA

11:15 AM – 12:00 PM	Panel Discussion	
Co-Moderator:	Manar Al-Ghabeish, PhD	Staff Fellow, DTP II, ORS, OGD, CDER, FDA
Co-Moderator:	Fang Wu, PhD	Senior Pharmacologist, DQMM, ORS, OGD, CDER, FDA
Panelists:	Tausif Ahmed, PhD	Head, Biopharmaceutics & Bioanalytical, Dr. Reddy's Laboratories
	Makarand Avachat, M. Pharm	Executive Vice-President, Pharmaceutical R&D, Lupin Ltd., India
	Lanyan Fang, PhD	Deputy Director, DQMM, ORS, OGD, CDER, FDA
	Rebeka Jereb, PhD	Scientist, Clinical Development, Sandoz
	Xiaojian Jiang, PhD	Deputy Director, DB II, OB, OGD, CDER, FDA
	Russ Rackley, PhD	Head, Global PK and Drug Metabolism, Viatrix
	Kimberly Raines, PhD	Branch Chief, Division of Biopharmaceutics, ONDP, OPQ, CDER, FDA
	Wei-Jhe Sun, PhD	Senior Pharmacologist, DTP II, ORS, OGD, CDER, FDA
	Yu Chung Tsang, PhD	Chief Scientific Officer, Biopharmaceutics & Biostatistics, Apotex Inc
	Ilan Zalit	Sr Director of Gx R&D, Teva Pharma
	Lei Zhang, PhD	Deputy Director, ORS, OGD, CDER, FDA

12:00 PM – 1:00 PM **Lunch Break**

Session 2: Parenteral (Injectable) Products

Sub-Session 2A: Enhancing the Efficiency of Bioequivalence Approaches for Generic Products with Complex Active Ingredients

This session will discuss what research is needed to improve methods for API and impurity (immunogenicity) characterizations, particularly for peptide and oligonucleotide products, and specifically related to the development of methods and standards for peptide immunogenicity bioassays. This session will also discuss what research is needed to advance comparative analysis of complex APIs, and associated considerations. Research into quantitative methods, modeling, simulation, and the development of AI/ML tools that can support the development of efficient BE approaches for generic products with complex APIs will specifically be discussed.

1:00 PM – 1:15 PM	Challenges and Opportunities for Innate Immunogenicity Assessment of Peptide Therapeutics	
	Andrew Graves, MS	Director, Immunogenicity Assessment, Teva Pharmaceutical Industries, Ltd
1:15 PM – 1:30 PM	Methods and Standards for Assessing the Immunogenicity Risk of Peptide APIs and Their Impurities	
	Anne De Groot, MD	CEO & CSO, EpiVax, Inc.
1:30 PM – 1:45 PM	Comparability Study of Generic Oligonucleotide Therapeutics	
	Dongyuan Wang, PhD	Program Manager, Synthron B.V.
1:45 PM – 2:30 PM	Panel Discussion	
Co-Moderator:	Cameron Smith, PhD	Branch Chief, DLBP I, OLDP, OPQ, CDER, FDA
Co-Moderator:	Deyi Zhang, PhD	Senior Chemist, DTP I, ORS, OGD, CDER, FDA
Panelists:	Kurt Brumbaugh, MS	Director, Biostatistics, Viatrix
	Anne De Groot, MD	CEO & CSO, EpiVax, Inc.
	Andrew Graves, MS	Director, Immunogenicity Assessment, Teva Pharmaceutical Industries, Ltd
	Viral Jogani, PhD	General Manager, R&D, Sun Pharmaceutical Industries, Ltd
	Daniela Verthelyi, MD, PhD	Laboratory Chief, OBP, OPQ, CDER, FDA
	Dongyuan Wang, PhD	Program Manager, Synthron B.V.

2:30 PM – 2:45 PM **Coffee Break**

Sub-Session 2B: Enhancing the Efficiency of Bioequivalence Approaches for Generic Dosage Forms and Formulations

This session will discuss what research is needed to improve methods for characterizing complex formulations and excipient effects, focusing on complex injectable products including LAI products; Q1 and Q2 formulation comparability challenges for complex and non-complex (e.g., injectable) products; contextualizing the roles of excipients in formulations; and conducting in vivo or in vitro studies to assess risks for excipients. This session will also discuss what research is needed to develop novel BE approaches for LAI products, focused on leveraging in vitro and in silico methods when appropriate; developing in vitro only BE approaches for products like phytonadione injectable emulsion; and characterizing complex polymeric ingredients. This session will also discuss what research is needed to address challenges related to the device constituent of injectable products and to facilitate the use of quantitative methods, modeling, simulation, or AI/ML tools to improve the efficiency of BE approaches for these complex dosage forms and formulations.

2:45 PM – 3:00 PM	LG Polymer Properties and Formulation Manufacturing Drive the Performance of Extended Release Drug Products	
	Tom Tice, PhD	Sr. Director for Global Strategic & Tech. Mkt., Evonik Nutrition & Care GmbH
3:00 PM – 3:15 PM	Challenges & Opportunities for the Development & Regulatory Evaluation of Long-Acting Injectable Drug Products	
	Stephan Schmidt, PhD, FCP	Prof., UF College of Pharmacy, Director, Center for Pmetrics & Sys. Pharmacol
3:15 PM – 3:30 PM	New PLGA Analytical Tools for Universal Reverse Engineering of Complex Long-Acting Injectable Formulations	
	Kinam Park, PhD	President, Akina, Inc., Prof., Pharmaceutics & Biomed Eng., Purdue University
3:30 PM – 3:45 PM	Future Directions for PK BE Studies of Long-Acting Injectables via Modeling and Simulation Approaches	
	Keith Gallicano, Ph.D	President, SAAMnow

3:45 PM – 4:30 PM

Panel Discussion

Co-Moderator: Lanyan (Lucy) Fang
Co-Moderator: Yan Wang

Deputy Director, DQMM, ORS, OGD, CDER, FDA
Lead Pharmacologist, DTP I, ORS, OGD, CDER, FDA

Panelists: Keith Gallicano, PhD
Ripen Misra, PhD
Kinam Park, PhD
Brian Sadler, PhD
Stephan Schmidt, PhD, FCP
Tom Tice, PhD
Feng Zhang, PhD
Shawn Zhang, Ph.D.
Liang Zhao, PhD

President, SAAMnow
Director Co-Development, Apotex
President, Akina, Inc., Prof., Pharmaceuticals & Biomed Eng., Purdue University
Sr. Scientific Director, Quantitative Pharmacol & Pmetrics, ICON plc
Prof., UF College of Pharmacy, Director, Center for Pmetrics & Sys. Pharmacol
Sr. Director for Global Strategic & Tech. Mkt., Evonik Nutrition & Care GmbH
Associate Prof. of Molecular Pharmaceuticals, Univ. of Texas at Austin
Managing Director, DigiM Solution LLC
Director, DQMM, ORS, OGD, CDER, FDA

End Day 1

Fiscal Year (FY) 2023 Generic Drug Science and Research Initiatives Public Workshop

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Agenda (Day 2)

9:00 AM – 9:15 AM **Opening Remarks**
Robert Lionberger, PhD Director, ORS, OGD, FDA

Session 3: Inhalation Products

Session 3: **Enhancing the Efficiency of Bioequivalence Approaches for Complex Generic Inhalation Products**

This session will discuss what research is needed to improve alternative BE approaches for OIDs as alternatives to FEV-1 endpoint studies, particularly for suspension or solution-based OIDs, and specifically including research to standardize methods for dissolution testing and equipment like mouth/throat models for OIDs. This session will also discuss what research and types of evidence are needed to justify other than minor differences in the device constituent of inhalation products, including research to address any emerging challenges for generics with transitioning to low global warming propellants. This session will also discuss what research is needed to facilitate the use of quantitative methods, modeling, simulation, or AI/ML tools to improve the efficiency of BE approaches for generic inhalation products.

9:15 AM – 9:30 AM **Alternate Bioequivalence Approaches: Validation of the Regional Lung Deposition of an Orally Inhaled Drug Product**
Clare Butler, PhD Principal Product Development Scientist, Teva Pharma

9:30 AM – 9:45 AM **Alternative In Vitro Bioequivalence Methods for Testing Generic Orally Inhaled Drug Products**
Nicholas Holtgrewe, PhD Chemist, DCDA, OTR, OPQ, CDER, FDA

9:45 AM – 10:00 AM **Transition to Low Global Warming Potential Propellants: Impacts on Equivalence**
Andrew Cooper, PhD Senior Director, Development for In Vivo Performance, Viatrix

10:00 AM – 10:45 AM **Panel Discussion**

Co-Moderator: Qing Liu, PhD Deputy Division Director, DB I, OB, OGD, CDER, FDA
Co-Moderator: Ross Walenga, PhD Chemical Engineer, DQMM, ORS, OGD, CDER, FDA

Panelists: Craig Bertha, PhD Chemist, DNDP II, ONDP, OPQ, CDER, FDA
Clare Butler, PhD Principal Product Development Scientist, Teva Pharma
Andrew Cooper, PhD Senior Director, Development for In Vivo Performance, Viatrix
Jan De Backer, PhD Chief Executive Officer, Fluidra NV
Ann Purrington, RPh, RAC Regulatory Affairs Director, Kindeva Drug Delivery
Nicholas Holtgrewe, PhD Chemist, DCDA, OTR, OPQ, CDER, FDA
Bing Li, PhD Associate Director for Science, OB, OGD, CDER, FDA

10:45 AM – 11:00 AM **Coffee Break**

Session 4: Topical Products

Session 4: **Enhancing the Efficiency of Bioequivalence Approaches for Complex Generic Topical Products**

This session will discuss what research is needed to improve alternative BE approaches for topical drug products, addressing challenges with implementing in vitro BE methods, and expanding efficient characterization-based BE approaches for Q3 similar topical generics. This session will also discuss what research is needed to facilitate the use of quantitative methods, modeling, simulation, or AI/ML tools to improve the efficiency of BE approaches for generic topical products.

11:00 AM – 11:05 AM **Overview**
Markham Luke, MD, PhD Director, DTP I, ORS, OGD, CDER, FDA

11:05 AM – 11:20 AM **Alternative In Vitro BE Methods for Topical Generic Products**
Sajeev Chandran, PhD, MBA Director, Pharmaceutical R&D, Lupin Ltd, India

11:20 AM – 11:35 AM **Challenges & Successes Integrating Characterization Data to Mechanistic Formulation Models of Skin Absorption**
James F. Clarke, PhD Senior Research Scientist, Certara UK, Simcyp Division

11:35 AM – 12:30 PM **Panel Discussion**

Co-Moderator: Priyanka Ghosh, PhD Lead Pharmacologist, DTP I, ORS, OGD, CDER, FDA
Co-Moderator: Eleftheria Tsakalozou, PhD Senior Pharmacologist/Acting Team Lead, DQMM, ORS, OGD, CDER, FDA

Public Comment: Jaya Abraham, PhD Sr. VP, Global Pharmaceutical Development, Glenmark Pharma Ltd, India
Panelists: Sajeev Chandran, PhD, MBA Director, Pharma R&D, Lupin Ltd, India
James F. Clarke, PhD Associate Principal Scientist, Certara UK, Simcyp Division

Mary Lee, MD
Markham Luke, MD, PhD
Shitalkumar Pathak, M. Pharma
Lakshmi Raghavan, PhD
Sam Raney, PhD
Jessica Spires, PhD
Hongling Zhang, PhD

Senior Physician, DCR, OSCE, OGD, CDER, FDA
Director, DTP I, ORS, OGD, CDER, FDA
Sr. VP, Analytical R&D, Glenmark Pharma Ltd, India
Founder & CEO at Healios Ventures
Associate Director for Science, ORS, OGD, CDER, FDA
Principal Scientist, Simulations Plus, Inc.
Director, DB II, OB, OGD, CDER, FDA

12:30 PM – 1:15 PM

Lunch Break

Session 5: Public Comments and Discussion

This session will focus on emerging industry perspectives about the challenges impacting generic product development that are the most critical to address during FY 2024. The presentations will discuss challenges associated with several prominent scientific issues impacting generic product development, and suggest how each of these issues might be addressed by focused research initiatives.

1:15 PM – 1:30 PM

Public Comments

Open Public Comment Period

1:30 PM – 2:15 PM

Panel Discussion

Moderator:

Robert Lionberger, PhD

Director, ORS, OGD, CDER, FDA

Panelists:

Jaya Abraham, PhD
Makarand Avachat, M. Pharm
Andrew Cooper, PhD
Martin Ehlert, PhD
Andrew Graves, MS
Ajay Jaysingh Khopade, PhD
Daniel Robins, PhD
Anna Schwendeman, PhD
Tom Tice, PhD

Sr. Vice-President, Global Pharm Dev, Glenmark Pharma Ltd, India
Executive Vice-President, Pharmaceutical R&D, Lupin Ltd, India
Senior Director, Development for In Vivo Performance, Viatris
Vice-president, Global API R&D, Apotex
Director, Immunogenicity Assessment, Teva Pharmaceutical Industries
Vice President, R&D at Sun Pharmaceutical Industries Ltd
President & CEO at Capstone Development Services Co. LLC
Co-Director, CRCG and Prof., University of Michigan
Sr. Director for Global Strategic & Tech. Mkt., Evonik Nutrition & Care GmbH

2:15 PM – 2:30 PM

Closing Remarks

Robert Lionberger, PhD

Director, ORS, OGD, CDER, FDA

End Day 2

Appendix of Abbreviations

AI	Artificial Intelligence
API	Active Pharmaceutical Ingredient
BE	Bioequivalence
B.V.	Besloten Vennootschap (closed company with limited liability)
Biomed	Biomedical
CEO	Chief Executive Officer
CDER	Center for Drug Evaluation and Research
Co.	Company
CRCG	Center for Research on Complex Generics
CSO	Chief Scientific Officer
DB I	Division of Bioequivalence I
DB II	Division of Bioequivalence II
DCDA	Division of Complex Drug Analysis
DCR	Division of Clinical Review
DLBP I	Division of Liquid Based Products I
DQMM	Division of Quantitative Methods and Modeling
DPQR	Division of Product Quality Research
DPTR	Division of Pharmacology/Toxicology Review
DTP I	Division of Therapeutic Performance I
DTP II	Division of Therapeutic Performance II
Eng.	Engineering
FEV-1	Forced Expiratory Volume in the First Second
F R&D	Formulation Research and Development
FDA	United States Food and Drug Administration
GDUFA	Generic Drug User Fee Amendments
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
Inc.	Incorporated
IR	Immediate Release
IT	Information Technology
LAI	Long-Acting Injectable
LG Polymer	Poly (Lactide-co-Glycolide) Polymer
LLC	Limited Liability Company
Ltd	Limited
Mkt.	Marketing
MD	Doctor of Medicine
ML	Machine Learning
M. Pharm	Master of Pharmacy
MS	Master of Science
NDSRI	Nitrosamine drug substance related impurity
NV	Naamloze Venootschap (public limited company)
OB	Office of Bioequivalence
OBP	Office of Biotechnology Products
OCP	Office of Clinical Pharmacology
OGD	Office of Generic Drugs
OIDP	Orally Inhaled Drug Products
OLDP	Office of Lifecycle Drug Products
ONDP	Office of New Drug Products
OPQ	Office of Pharmaceutical Quality
ORS	Office of Research and Standards
OSCE	Office of Safety and Clinical Evaluation
OTR	Office of Testing and Research
OTS	Office of Translational Sciences
Pharma	Pharmaceuticals
Pharmacol	Pharmacology
PhD	Doctor of Philosophy
Pmetrics	Pharmacometrics
PK	Pharmacokinetics
Plc	Private limited company
PLGA	Poly(lactic-co-Glycolic Acid)
Prof.	Professor
Q1	Qualitative
Q2	Quantitative
Q3	Physicochemical and structural (arrangement of matter)
QA	Quality Assurance
R&D	Research and Development
RPh	Registered Pharmacist
RAC	Regulatory Affairs Certification
SAAMnow	Scientists Advancing Affordable Medicines, Inc.
Sr.	Senior
Sys.	Systems
Tech.	Technical
UCSF	University of California, San Francisco
UF	University of Florida
UK	United Kingdom
Univ.	University
VP	Vice President