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, Viatris
	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, Synthon 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, Viatris
	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, Synthon 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, SAAM*now*

3:45 PM – 4:30 PM	***Panel Discussion***		
	Co-Moderator:	Lanyan (Lucy) Fang	Deputy Director, DQMM, ORS, OGD, CDER, FDA
	Co-Moderator:	Yan Wang	Lead Pharmacologist, DTP I, ORS, OGD, CDER, FDA
	Panelists:	Keith Gallicano, PhD	President, SAAM*now*
		Ripen Misra, PhD	Director Co-Development, Apotex
		Kinam Park, PhD	President, Akina, Inc., Prof., Pharmaceutics & Biomed Eng., Purdue University
		Brian Sadler, PhD	Sr. Scientific Director, Quantitative Pharmacol & Pmetrics, ICON plc
		Stephan Schmidt, PhD, FCP	Prof., UF College of Pharmacy, Director, Center for Pmetrics & Sys. Pharmacol
		Tom Tice, PhD	Sr. Director for Global Strategic & Tech. Mkt., Evonik Nutrition & Care GmbH
		Feng Zhang, PhD	Associate Prof. of Molecular Pharmaceutics, Univ. of Texas at Austin
		Shawn Zhang, Ph.D.	Managing Director, DigiM Solution LLC
		Liang Zhao, PhD	Director, DQMM, ORS, OGD, CDER, FDA

End Day 1

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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 OIDPs as alternatives to FEV-1 endpoint studies, particularly for suspension or solution-based OIDPs, and specifically including research to standardize methods for dissolution testing and equipment like mouth/throat models for OIDPs. 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, Viatris
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, Viatris
	Jan De Backer, PhD	Chief Executive Officer, Fluidda 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	Senior Physician, DCR, OSCE, OGD, CDER, FDA
	Markham Luke, MD, PhD	Director, DTP I, ORS, OGD, CDER, FDA
	Shitalkumar Pathak, M. Pharma	Sr. VP, Analytical R&D, Glenmark Pharma Ltd, India
	Lakshmi Raghavan, PhD	Founder & CEO at Healios Ventures
	Sam Raney, PhD	Associate Director for Science, ORS, OGD, CDER, FDA
	Jessica Spires, PhD	Principal Scientist, Simulations Plus, Inc.
	Hongling Zhang, PhD	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	Sr. Vice-President, Global Pharm Dev, Glenmark Pharma Ltd, India
	Makarand Avachat, M. Pharm	Executive Vice-President, Pharmaceutical R&D, Lupin Ltd, India
	Andrew Cooper, PhD	Senior Director, Development for In Vivo Performance, Viatris
	Martin Ehlert, PhD	Vice-president, Global API R&D, Apotex
	Andrew Graves, MS	Director, Immunogenicity Assessment, Teva Pharmaceutical Industries
	Ajay Jaysingh Khopade, PhD	Vice President, R&D at Sun Pharmaceutical Industries Ltd
	Daniel Robins, PhD	President & CEO at Capstone Development Services Co. LLC
	Anna Schwendeman, PhD	Co-Director, CRCG and Prof., University of Michigan
	Tom Tice, PhD	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	Polylactic-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
SAAM*now*	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