In Vitro Release Test (IVRT) and In Vitro Permeation Test (IVPT) Methods

Best Practices and Scientific Considerations for ANDA Submissions

Virtual Public Workshop

August 18th, 19th, and 20th

2021

Agenda

IVRT and IVPT are important methods used by the generic drug industry and in other contexts to support demonstrations of bioequivalence for generic topical drug products, evaluations of the heat effects and product quality for generic transdermal delivery systems (also known as patches), assessments of the bioavailability of ingredients in sunscreen products, and characterization of other biopharmaceutical aspects of topical and transdermal generic drug products.

The purpose of this workshop is to discuss the scientific principles and practical considerations that inform current FDA thinking and USP recommendations for IVRT and IVPT studies, explore challenging issues that would benefit from broader discussion[1], identify areas that would benefit from further research, and discuss opportunities for coordination and collaboration between the FDA, USP, academic institutions, product manufacturers, diffusion cell equipment manufacturers, contract research organizations, consultants and other stakeholders.

FDA and the Center for Research on Complex Generics, which is a collaboration between the University of Maryland School of Pharmacy and the University of Michigan College of Pharmacy, are dedicated to advancing programs that stimulate scientific dialogue, disseminate current insights about complex generics, and generate new knowledge in support of FDA's mission to promote and protect the public health by increasing access to safe and effective generic medicines.

GENERAL TOPICS THAT WILL BE THE FOCUS OF THE WORKSHOP:

- IVRT study designs in different contexts including supporting a demonstration of bioequivalence for topical generics, scale-up and post-approval changes, and different dosage forms
- IVPT study designs in different contexts including supporting a demonstration of bioequivalence for topical generics, heat effects for topical or transdermal delivery systems, and bioavailability for sunscreen products
- Challenges with aberrant data, outliers, inclusion/exclusion criteria, and statistical analysis of IVPT data
- Theoretical principles and practical challenges with IVRT and IVPT method development, validation, and transfer
- Operational principles and practical challenges for IVRT and IVPT diffusion cell apparatus
- Submission of IVRT and IVPT information in Abbreviated New Drug Applications (ANDAs), including reportable information, format of data/results, organization of information, and common deficiencies
- Quality management systems, retention samples, laboratory qualification, documentation, and inspections for IVRT and IVPT studies submitted in ANDAs

[1] During '**Talk Show Style**' panel discussions, panelists will systematically address a series of specific topics that would benefit from a broader discussion among experts, representing perspectives of different stakeholders. For each topic, the moderator will provide a brief introduction/overview of the key issues relevant that topic, followed by a roundtable style discussion in which panelists will deliberate on the challenges and describe corresponding (situational) best practices, before moving on to the next topic. Specific topics and issues to be addressed in each '**Talk Show Style**' panel discussion will be announced closer to the event date.

Day 1: August 18, 2021

8:30 AM – 8:45 AM	**Welcome and Opening Remarks**	
	James Polli, PhD	Co-Director, CRCG
	Anna Schwendeman, PhD	Co-Director, CRCG
8:45 AM – 9:00 AM	**Keynote Address**	
	The In Vitro Permeation Test (IVPT): Historical Perspective, Current Context, and Future Directions	
	Howard Maibach, MD	Professor of Dermatology, University of California, San Francisco
9:00 AM – 10:00 AM	**Foundation Lecture**	
	IVPT Fundamentals: Scientific and Practical Considerations	
	Sam Raney, PhD	Associate Director for Science, ORS, OGD, FDA
10:00 AM – 10:15 AM	***Coffee Break***	
	Scientific and Regulatory Uses of IVPT Studies	
10:15 AM – 10:30 AM	***IVPT Studies with Sunscreen Products: Experimental Parameters***	
	Yang Yang, PhD	Staff Fellow, DPQR, OTR, OPQ, FDA
10:30 AM – 10:45 AM	***IVPT Studies with Sunscreen Products: Potential Regulatory Utility***	
	E. Dennis Bashaw, PharmD	Senior Science Advisor, OCP, OTS, FDA (retired)
10:45 AM – 11:15 AM	***IVPT Studies with Topical and Transdermal Products***	
	Audra Stinchcomb, PhD	Professor of Pharmaceutical Sciences, University of Maryland, Baltimore
11:15 AM – 11:45 AM	***Q&A Session with Panel***	
Moderator:	**Bozena Michniak-Kohn, PhD**	Professor of Pharmaceutics, Rutgers University
Panelists:	**Audra Stinchcomb, PhD**	Professor of Pharmaceutical Sciences, University of Maryland, Baltimore
	E. Dennis Bashaw, PharmD	Senior Science Advisor, OCP, OTS, FDA (retired)
	Markham Luke, MD, PhD	Director, DTP-I, ORS, OGD, FDA
	Howard Maibach, MD	Professor of Dermatology, University of California, San Francisco
	Paul Lehman, MS	Vice President and Head of Dermal and Transdermal Research, QPS, LLC
	Ajay Banga, PhD	Professor and Chair of Pharmaceutical Sciences, Mercer University
	Sam Raney, PhD	Associate Director for Science, ORS, OGD, FDA
	Yang Yang, PhD	Staff Fellow, DPQR, OTR, OPQ, FDA
11:45 AM – 12:30 PM	***Lunch Break***	
	IVPT Method Development, Validation, and Transfer	
12:30 PM – 1:00 PM	***IVPT Studies During Topical Product Development***	
	Leandro Santos, PhD	Director for Clinical Research, Incyte
1:00 PM – 3:00 PM	***Talk Show Style*** [1] ***Panel Discussion***	
Moderator:	**Hiren Patel, PhD**	Staff Fellow, DB-II, OB, OGD, FDA
Panelists:	**Leandro Santos, PhD**	Director for Clinical Research, Incyte
	Jon Lenn, PhD	Chief Scientific Officer, MedPharm Ltd.
	Vijendra Nalamothu, PhD	Chairman and Chief Executive Officer, Tergus Pharma
	Paul Lehman, MS	Vice President and Head of Dermal and Transdermal Research, QPS, LLC
	Narasimha Murthy, PhD	Professor of Pharmaceutics, University of Mississippi
	Audra Stinchcomb, PhD	Professor of Pharmaceutical Sciences, University of Maryland, Baltimore
	Sam Raney, PhD	Associate Director for Science, ORS, OGD, FDA
	Abhishek Juluri, PhD	Staff Fellow, DB-III, OB, OGD, FDA
3:00 PM – 3:15 PM	***Coffee Break***	
	IVPT Data Challenges and Statistical Analysis	
3:15 PM – 3:35 PM	***IVPT Data Challenges in the Real World***	
	Paul Lehman, MS	Vice President and Head of Dermal and Transdermal Research, QPS, LLC
3:35 PM – 4:00 PM	***IVPT Data Analysis and Statistics***	
	Elena Rantou, PhD	Lead Mathematical Statistician, DB-VII, OB, OTS, FDA
4:00 PM – 5:00 PM	***Talk Show Style*** [1] ***Panel Discussion***	
Moderator:	**Priyanka Ghosh, PhD**	Staff Fellow, DTP-I, ORS, OGD, FDA
Panelists:	**Paul Lehman, MS**	Vice President and Head of Dermal and Transdermal Research, QPS, LLC
	Charles Bon, MS	President, Biostudy Solutions LLC
	Pina D'Angelo, MSc	Vice President, Biometrics, Innovaderm Research Inc.
	Sam Raney, PhD	Associate Director for Science, ORS, OGD, FDA
	Elena Rantou, PhD	Lead Mathematical Statistician, DB-VII, Office of Biostatistics, OTS, FDA
	Stella Grosser, PhD	Director, DB-VII, Office of Biostatistics, OTS, FDA
	Yuzhuo Pan, PhD	Pharmacologist, DB-II, OB, OGD, FDA
	Hiren Patel, PhD	Staff Fellow, DB-II, OB, OGD, FDA

Day 2: August 19, 2021

8:30 AM – 8:45 AM	**Welcome and Opening Remarks**	
	James Polli, PhD	Co-Director, CRCG
	Anna Schwendeman, PhD	Co-Director, CRCG
8:45 AM – 9:00 AM	**Keynote Address**	
	The In Vitro Release Test (IVRT): Historical Perspective, Current Context, and Future Directions	
	Vinod Shah, PhD	Consultant, VPS Consulting, LLC
9:00 AM – 10:00 AM	**Foundation Lecture**	
	IVRT Fundamentals: Scientific and Practical Considerations	
	Sam Raney, PhD	Associate Director for Science, ORS, OGD, FDA
10:00 AM – 10:15 AM	***Coffee Break***	
	U.S. Pharmacopeia (USP) General Chapters <1724> and <1002>	
10:15 AM – 10:30 AM	***USP General Chapter Revision Process***	
	Margareth Marques, PhD	Principal Scientific Liaison, USP
10:30 AM – 11:00 AM	***USP <1724> and <1002> Prospective Scope and Content***	
	Leandro Santos, PhD	Director for Clinical Research, Incyte
11:00 AM – 12:00 PM	***Q&A Session with Panel***	
Moderator:	**Kailas Thakker, PhD**	President, TopiKail Consulting
Panelists:	**Margareth Marques, PhD**	Principal Scientific Liaison, USP
	Leandro Santos, PhD	Director for Clinical Research, Incyte
	Kevin Warner, PhD	Vice President, Pharmaceutical Development, Alucent Biomedical, Inc.
	Sam Raney, PhD	Associate Director for Science, ORS, OGD, FDA
	Ashvin Patel, PhD	Director, Analytical Research and Business Development, Teledyne
	John Heaney, BS	Quality Manager, Quality Lab Accessories
	Tapash Ghosh, PhD	Pharmacologist, DB, ONDP, OPQ, FDA
12:00 PM – 1:00 PM	***Lunch Break***	
	IVRT Method Development, Validation, and Transfer	
1:00 PM – 1:25 PM	***Key Aspects in Developing Appropriate IVRT Methods for Topical Generic Products: Advances and Challenges***	
	Theo Kapanadze, PhD	Chief Science Officer, Diteba
1:25 PM – 1:50 PM	***IVRT Studies During Topical Product Development: Lifecycle Management for SUPAC-SS and Generics***	
	Cristina Yen, BS	Senior Manager, IVRT, Tergus Pharma
1:50 PM – 2:15 PM	***IVRT Studies During Topical Product Development: Challenges in Method Development and Transfer***	
	Kailas Thakker, PhD	President, TopiKail Consulting
2:15 PM – 2:30 PM	***Coffee Break***	
2:30 PM – 4:30 PM	***Talk Show Style*** [1] ***Panel Discussion***	
Moderator:	**Tannaz Ramezanli, PharmD, PhD**	Pharmacologist, DTP-I, ORS, OGD, FDA
Panelists:	**Cristina Yen, MS**	Senior Manager, IVRT, Tergus Pharma
	Theo Kapanadze, PhD	Chief Science Officer, Diteba
	Kailas Thakker, PhD	President, TopiKail Consulting
	Kevin Warner, PhD	Vice President, Pharmaceutical Development, Alucent Biomedical, Inc.
	Sam Raney, PhD	Associate Director for Science, ORS, OGD, FDA
	Hiren Patel, PhD	Staff Fellow, DB-II, OB, OGD, FDA
	Josephine Aimiuwu, PhD	Pharmacologist, DB-II, OB, OGD, FDA
	Abhishek Juluri, PhD	Staff Fellow, DB-III, OB, OGD, FDA

Day 3: August 20, 2021

9:00 AM – 9:15 AM	**Welcome and Opening Remarks**	
	James Polli, PhD	Co-Director, CRCG
	Anna Schwendeman, PhD	Co-Director, CRCG
	Diffusion Cell Apparatus	
9:15 AM – 9:45 AM	***Diffusion Cell Apparatus: Scientific Principles and Practical Challenges I***	
	Ahmed Zidan, PhD	Senior Staff Fellow, DPQR, OTR, OPQ, FDA
9:45 AM – 10:15 AM	***Diffusion Cell Apparatus: Scientific Principles and Practical Challenges II***	
	Jon Lenn, PhD	Chief Scientific Officer, MedPharm Ltd.
10:15 AM – 10:45 AM	***Diffusion Cell Apparatus: Considerations for Design and Use I***	
	Ashvin Patel, PhD	Director, Analytical Research and Business Development, Teledyne
10:45 AM – 11:15 AM	***Diffusion Cell Apparatus: Considerations for Design and Use II***	
	Luke Lee, PhD	President, Logan Instruments Corp.
11:15 AM – 12:00 PM	***Q&A Session with Panel***	
Moderator:	**Rong Wang, PhD**	Lead Pharmacologist, DB-I, OB, OGD, FDA
Panelists:	**Jon Lenn, PhD**	Chief Scientific Officer, MedPharm Ltd.
	Ashvin Patel, PhD	Director, Analytical Research and Business Development, Teledyne
	Luke Lee, PhD	President, Logan Instruments Corp.
	Andrew Wilt, BS	President, PermeGear, Inc.
	Kailas Thakker, PhD	President, TopiKail Consulting
	Sam Raney, PhD	Associate Director for Science, ORS, OGD, FDA
	Narasimha Murthy, PhD	Professor of Pharmaceutics, University of Mississippi
	Ahmed Zidan, PhD	Senior Staff Fellow, DPQR, OTR, OPQ, FDA
12:00 PM – 1:00 PM	***Lunch Break***	
	Submission of Information in Abbreviated New Drug Applications (ANDAs)	
1:00 PM – 1:30 PM	***Considerations for IVRT Data and Information Submitted in ANDAs***	
	Tian Ma, PhD	Staff Fellow, DB-I, OB, OGD, FDA
1:30 PM – 2:00 PM	***Considerations for IVPT Data and Information Submitted in ANDAs***	
	Archana Manerikar, MS, PharmD	Pharmacologist, DB-I, OB, OGD, FDA
2:00 AM – 2:30 PM	***Q&A Session with Panel***	
Moderator:	**Usha Katragadda, PhD**	Staff Fellow, DB-III, OB, OGD, FDA
Panelists:	**Tian Ma, PhD**	Staff Fellow, DB-I, OB, OGD, FDA
	Archana Manerikar, MS, PharmD	Pharmacologist, DB-I, OB, OGD, FDA
	Xiaojian Jiang, PhD	Deputy Director, DB-II, OB, OGD, FDA
	Anil Nair, PhD	Team Leader, DB-II, OB, OGD, FDA
	Juhyun Kim, PhD	Staff Fellow, DB-III, OB, OGD, FDA
	Hiren Patel, PhD	Staff Fellow, DB-II, OB, OGD, FDA
	Priyanka Ghosh, PhD	Staff Fellow, DTP-I, ORS, OGD, FDA
	Sam Haidar, PhD	Senior Science Advisor, OSIS, OTS, FDA
2:30 PM – 2:45 PM	***Coffee Break***	
	Quality Management Systems (QMS)	
2:45 PM – 3:15 PM	***QMS: Study Integrity Considerations***	
	Sam Haidar, PhD	Senior Science Advisor, OSIS, OTS, FDA
3:15 PM – 3:45 PM	***QMS: Industry Perspectives***	
	Kendall Powell, PhD	Senior Director of Bioanalytical, MedPharm Ltd.
3:45 PM – 4:30 PM	***Q&A Session with Panel***	
Moderator:	**Sam Haidar, PhD**	Senior Science Advisor, OSIS, OTS, FDA
Panelists:	**Kendall Powell, PhD**	Senior Director of Bioanalytical, MedPharm Ltd.
	Sam Raney, PhD	Associate Director for Science, ORS, OGD, FDA
	Priyanka Ghosh, PhD	Staff Fellow, DTP-I, ORS, OGD, FDA
	Paul Lehman, MS	Vice President and Head of Dermal and Transdermal Research, QPS, LLC
	Joseph Payne, BS	Vice President Quality and Compliance, Tergus Pharma
	Theo Kapanadze, PhD	Chief Science Officer, Diteba
	Amanda Jones, PhD	Lead Pharmacologist, DB-I, OB, OGD, FDA
	Hiren Patel, PhD	Staff Fellow, DB-II, OB, OGD, FDA
4:30 PM – 4:45 PM	**Workshop Summation**	
	Sam Raney, PhD	Associate Director for Science, ORS, OGD, FDA
4:45 PM – 5:00 PM	**Closing Remarks**	
	James Polli, PhD	Co-Director, CRCG
	Anna Schwendeman, PhD	Co-Director, CRCG

Appendix of Abbreviations

ANDA	Abbreviated New Drug Application
CRCG	Center for Research on Complex Generics
BS	Bachelor of Science
DB	Division of Biopharmaceutics
DB-I	Division of Bioequivalence I
DB-II	Division of Bioequivalence II
DB-III	Division of Bioequivalence III
DB-VIII	Division of Biostatistics VIII
DPQR	Division of Product Quality Research
DTP-I	Division of Therapeutic Performance I
FDA	United States Food and Drug Administration
IVRT	In Vitro Release Test
IVPT	In Vitro Permeation Test
LLC	Limited Liability Corporation
Ltd.	Limited
MD	Doctor of Medicine
MS	Master of Science
OB	Office of Bioequivalence
OCP	Office of Clinical Pharmacology
OGD	Office of Generic Drugs
ONDP	Office of New Drug Products
OPQ	Office of Pharmaceutical Quality
ORS	Office of Research and Standards
OSIS	Office of Study Integrity and Surveillance
OTR	Office of Testing and Research
OTS	Office of Translational Sciences
PharmD	Doctor of Pharmacy
PhD	Doctor of Philosophy

[1] During '**Talk Show Style**' panel discussions, panelists will systematically address a series of specific topics that would benefit from a broader discussion among experts, representing perspectives of different stakeholders. For each topic, the moderator will provide a brief introduction/overview of the key issues relevant that topic, followed by a roundtable style discussion in which panelists will deliberate on the challenges and describe corresponding (situational) best practices, before moving on to the next topic. Specific topics and issues to be addressed in each '**Talk Show Style**' panel discussion will be announced closer to the event date.