

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

## **Best Practices and Scientific Considerations for ANDA Submissions**

**Virtual Public Workshop**  
August 18<sup>th</sup>, 19<sup>th</sup>, and 20<sup>th</sup>  
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<sup>1</sup>, 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

---

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

**Day 2:****August 19, 2021**

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

**Day 3:****August 20, 2021**

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

---

<sup>1</sup> 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.