The Evolution of Biopharmaceutics: Risk Assessment and Clinical Relevance

Public Workshop
April 30-May 1, 2026
Agenda

Thursday, April 30
Day 1

7:45 AM – 8:30 AM ***Registration***

Session 1: Biopharmaceutics Risk Assessment Framework
Session Leads: Dr. Helena Engman and Dr. Hailing Zhang
Scope: This foundational session introduces a science- and risk-based framework for linking in vitro dissolution testing to in vivo clinical performance. It highlights the evolution of dissolution from a traditional quality control tool to a predictive, patient-centric measure of bioperformance that can inform regulatory and development decisions. The session will outline the scientific principles connecting API physicochemical properties, formulation factors, and gastrointestinal physiology to drug absorption. It will describe a structured Biopharmaceutics Risk Assessment Framework designed to systematically identify, rank, and mitigate biopharmaceutic risk, and to align the level of supporting evidence with the degree of potential clinical impact. Emerging laboratory and analytical approaches that enhance prediction of in vivo performance will also be discussed. Overall, the session establishes a strategic foundation for integrating predictive dissolution into modern drug product development, regulatory assessment, and lifecycle management to support consistent clinical performance and patient-centric quality standards.

8:30 AM – 8:35 AM ***Welcome and Speaker Introductions***
Hailing Zhang, PhD Division Director, DPQA XII, OPQA II, OPQ, CDER, FDA

8:35 AM – 8:55 AM ***Keynote: The Evolution of Dissolution Testing: Toward Prediction of In Vivo Performance***
Lawrence X. Yu, PhD Director, OPQA II, OPQ, CDER, FDA; Adjunct Professor, Univ. of Michigan

Dissolution testing is evolving from a quality control tool to a predictive method that discriminates between bioequivalent and non-bioequivalent batches, serving as a reliable surrogate for in vivo performance. This approach enhances understanding of how critical material attributes and process parameters influence therapeutic outcomes, supporting more precise product and process knowledge. Ultimately, predictive dissolution establishes science- and risk-based, patient-centric quality standards that maintain product safety and efficacy while strengthening the scientific basis for regulatory decisions.

8:55 AM – 9:15 AM ***Current Biopharmaceutical Risk Assessment Practices in New Drug Product Development of Solid Oral Dosage Forms***
Filippos Kesisoglou, PhD, FAAPS Scientific Associate VP, Pharmaceutical Sciences, Merck & Co,. Inc.

Dissolution specifications are a key component of the control strategy for solid oral dosage forms and are a mandatory element of drug product development and new product registration. In practice, dissolution methods designed with appropriate sensitivity to critical biopharmaceutic attributes are frequently challenged during regulatory review, leading to considerable back-and-forth, potential delays in product approval and launch, and, in some cases, divergent specifications for the same product across regions. This presentation will describe how biopharmaceutic risks are systematically identified, assessed, and mitigated throughout development. The focus will be on integrating biopharmaceutic risk assessment into the overall control strategy so that dissolution testing becomes a clinically meaningful, risk-based tool that robustly supports product development, regulatory decision-making, and life-cycle management.

9:15 AM – 9:35 AM ***Underutilized and Recent Laboratory and Data Analysis Approaches to Assess Oral Biopharmaceutics Risk***
James Polli, PhD Professor and Ralph F. Shangraw/Noxell Endowed Chair in Industrial Pharmacy and Pharmaceutics, University of Maryland School of Pharmacy

This presentation will discuss underutilized and recent methods to assess oral biopharmaceutics risk. Laboratory methods include non-compendial dissolution methods, techniques that elucidate in vitro release mechanism and susceptibility to formulation/process factors, and in vivo human formulation PK studies. Data analysis approaches include deconvolution-based methods that assess the role of release in overall drug absorption kinetics.

9:35 AM – 9:55 AM ***Predictive Biopharmaceutics: A Deep Dive into the Risk Assessment Framework***
Bhagwant Rege, PhD Division Director, DPQA VI, OPQA I, OPQ, CDER, FDA

This presentation introduces a Biopharmaceutics Risk Assessment Framework designed to link in vitro dissolution to its clinical performance. The framework evaluates key factors like the drug's properties, its formulation, and physiological conditions in the gastrointestinal tract in couple with pharmacokinetic data whenever necessary and rank products by risk, from "very low" to "very high." This risk level determines the amount of evidence required to develop an in vitro dissolution method that can be used to predict in vivo performance to achieve patient-centric quality standards. The main objective is to develop predictive dissolution tests that guarantee consistent clinical performance through the lifecycle.

9:55 AM – 10:00 AM ***Session 1 Summary***
Helena Engman, MSc, PhD Senior Principal Scientist, ADME Sciences, Seda Pharmaceutical Development Services

10:00 AM – 10:15 AM ***Break***

Session 2: High Risk Drug Products-IVIVC and IVIVR

Session Leads: Dr. James Polli, Dr. Filippos Kesisoglou, and Dr. Haritha Mandula

Scope: This session focuses on products where rate and extent of drug absorption are dictated by in vivo drug release. Discussions will cover mitigation strategies including PK studies to establish IVIVRs, and when possible validated IVIVCs, the development of "Bioequivalence Safe Spaces," and the supplementary role of Physiologically Based Biopharmaceutics Modeling (PBBM).

10:15 AM – 10:20 AM ***Speaker Introductions***
Haritha Mandula, PhD Acting Supervisor, DPQA VI, OPQA I, OPQ, CDER, FDA

10:20 AM – 10:40 AM ***High-Risk Drug Products and In Vivo Release: Defining the BE Safe Space Through IVIVC/IVIVR Development***
Rajesh Savkur, PhD Senior Biologist, DPQA VI, OPQA I, OPQ, CDER, FDA

This presentation is aimed at addressing the regulatory framework for drug products where the pharmacokinetics and in vivo performance are controlled by in vivo drug release. It examines high-risk product classification and associated regulatory expectations, describes IVIVR and IVIVC as decision-making tools, and presents a framework for establishing a "Bioequivalence Safe Space" that defines acceptable performance boundaries and establishes clinical relevance.

10:40 AM – 11:00 AM ***Linking In Vitro Dissolution to In Vivo Performance of Extended-Release Drug Products***
Yihong Qiu, PhD Chief Technical Director, QPD Solutions

This presentation will address the challenges, strategies, and key considerations in linking in vitro and in vivo data for oral extended-release (ER) dosage forms, based on an integrated understanding of API's properties, ER technologies, formulation design, and dissolution methodologies. Case studies will include the development of predictive dissolution methods and the use of IVIVC to ensure the quality and performance of marketed products.

11:00 AM – 11:20 AM ***Understanding In Vitro Dissolution and Clinical Performance for High-Risk IR Products***
Sanjaykumar Patel, PhD Senior Principal Scientist, Merck & Co., Inc.

This presentation will address biopharmaceutics risk assessment strategies for high-risk immediate release formulations such as amorphous solid dispersions. Examples will be used to demonstrate the interrogation of key CQAs in vitro and their subsequent assessment in a clinical relative bioavailability study towards establishment of IVIVR and/or safe space.

11:20 AM – 11:40 AM ***Development of a Dissolution Control Strategy and BE Safe-Space for a Solid-Dispersion Drug Product***
David Sperry, PhD Executive Director, Synthetic Molecule Design & Development, Eli Lily

This case study presents an amorphous solid dispersion drug product where extensive investigations demonstrated that the drug substance does not crystallize and that tablet erosion controls the release mechanism. A dissolution method was developed to be sensitive to erosion-related parameters. Pharmacokinetic data confirmed dose-proportional absorption across all strengths regardless of dissolution rate of the administered dosage form, establishing a dissolution safe-space that could justify specifications.

11:40 AM – 11:45 AM ***Session 2 Summary***
Haritha Mandula, PhD Acting Supervisor, DPQA VI, OPQA I, OPQ, CDER, FDA

11:45 AM – 12:45 PM ***Lunch Break***

Session 3: Medium Risk Drug Products-How to Use Biopharmaceutics Tool to Understand and Mitigate Risk?

Session Leads: Dr. Emilija Fredro-Kumbaradzi, Dr. Duxin Sun, Dr. Hailing Zhang, Dr. Ahmed Zidan

Scope: This session addresses products where in vivo dissolution and absorption are governed by drug substance properties and are likely impacted by GI physiological conditions. The focus will be on developing dissolution methods, including biorelevant methods that mimic and may therefore be, indicative of in vivo performance, the potential for these methods to exist separately from QC dissolution methods, and their use in mitigating BA/BE requirements for lifecycle management. Discussions will center on what data and scientific justifications are required to potentially downgrade, rather than just mitigate, the risk from medium to low from a regulatory perspective and therefore, reduce the dissolution testing requirements throughout the product's lifecycle.

12:45 PM – 12:50 PM ***Speaker Introductions***
Duxin Sun, PhD Associate Dean for Research, The Charles R. Walgreen Jr. Professor of Pharmacy & Pharmaceutical Sciences, College of Pharmacy, The University of Michigan

12:50 PM – 1:10 PM ***The Tale of Truqap Dissolution: The Apex of Science vs. Compliance***
James Mann, MSci, PhD Principal Scientist, In Vitro Product Performance, AstraZeneca

The talk will discuss the dissolution method development story for Truqap (capivasertib – BCS IV) and the link to in vivo performance and the discriminatory power of the method. The final regulatory positions from the main health authorities and the reasons for differing opinions discussed.

1:10 PM – 1:30 PM ***Capturing Fasting Gastric Motility and pH Variability In Vitro to De-Risk Development of Oral Medicines***
Dorota Danielak, PhD, dr hab Senior R&D Specialist, Physiolution

This presentation explores how fasting intake conditions — specifically gastric motility, pH, as well as temperature gradients, and non-linear emptying kinetics can be faithfully recreated in vitro to study drug dissolution. Through a case study, we reveal how these physiological factors can significantly influence the performance of an oral immediate-release capsule, offering key insights into in vivo pharmacokinetic variability and strategies to de-risk the development of oral medicines.

1:30 PM – 1:50 PM ***Biopharmaceutic Risk Assessment of a Neutral BCS Class IV Drug: A Generic Industry Perspective***
Emilija Fredro-Kumbaradzi, PhD Director, Biopharmaceutics & Statistics, R&D, Apotex, Inc.

This prestation will discuss the biopharmaceutics risk assessment in generic drug development involving evaluating innovator product complexity and establishing dissolution conditions based on API properties and GI tract performance. A BCS Class IV case study illustrates the integrated approach using bio-indicative dissolution methods, particle size modeling, and totality-of-evidence to mitigate biopharmaceutics risks.

1:50 PM – 2:10 PM ***Defining and Managing Medium-Risk Drug Products Within the Risk-Based Biopharmaceutics Framework: An FDA Perspective***
Hailing Zhang, PhD Division Director, DPQA XII, OPQA II, OPQ, CDER, FDA

This presentation will outline the FDA's perspective on medium-risk drug products whose dissolution and absorption are affected by gastrointestinal (GI) conditions. It will focus on integrating our understanding of the interplay between the drug product and GI conditions (pH variability, bile salt concentrations, food effects) into the risk assessment process for regulatory evaluation. Biorelevant dissolution methods validated by physiologically-based biopharmaceutics modeling (PBBM) will be discussed as a valuable tool to mitigate bioavailability/bioequivalence (BA/BE) study requirements for drug product lifecycle management. A case study will be presented to illustrate how biorelevant dissolution coupled with PBBM were developed and validated for a medium-risk drug product to ensure bioperformance and support regulatory decision-making.

2:10 PM – 2:15 PM ***Session 3 Summary***
Ahmed Zidan, PhD Senior Pharmacologist, DPQR V, OPQR, OPQ, CDER, FDA

Breakout Sessions: Framework, High Risk, Medium Risk

2:15 PM – 2:20 PM ***Transition to Breakout Session Rooms***

2:20 PM – 2:30 PM ***Introduction to Breakout Sessions Topic A and B***
Breakout Session by Moderators

2:30 PM – 3:30 PM ***Breakout Session A:*** Implementing Biopharmaceutics Risk Assessment Framework: Practical Strategies for Drug Development and Regulatory Decision-Making

***Breakout Session B*:** A Framework for Biopharmaceutics Risk Characterization and Mitigation Strategies for High-Risk Drug Products with Emphasis on Clinical Relevance

3:30 PM – 3:45 PM	***Break***
3:45 PM – 3:50 PM	***Transition to Breakout Session Rooms***
3:50 PM – 4:00 PM	***Introduction to Breakout Sessions Topic C and D*** **Breakout Session by Moderators**
4:00 PM – 5:00 PM	***Breakout Session C:*** What Biopharmaceutics Characteristics Differentiate a Medium Risk Product from a Low or High Risk Product? ***Breakout Session D:*** What Would be the Appropriate Control Strategy for Medium Risk Products to Ensure Bioperformance?
5:00 PM – 5:15 PM	***Day 1 Closing Remarks*** **Helena Engman, PhD** Senior Principal Scientist, ADME Sciences, Seda Pharmaceutical Development Services

Friday, May 1
Day 2

7:45 AM – 8:30 AM ***Registration***

8:30 AM – 8:45 AM ***Day 2 Welcome and Day 1 Recap***
Giuseppe Randazzo, MS Senior VP, Sciences & Regulatory Affairs, Association for Accessible Medicines

Session 4: Low and Very Low Risk Products-What is Needed and What is Not
Session Leads: Dr. Biljana Jankovic and Dr. Hardikkumar Patel
Scope: This session examines products where in vivo dissolution is minimally impacted by formulation variables or GI conditions. For very low-risk products, discussions will explore the potential for waiving dissolution testing for batch release. For low-risk products, the session will cover how simple dissolution tests are sufficient to ensure consistent PK performance and what minimal development data are required.

8:45 AM – 8:50 AM ***Speaker Introductions***
Carrie Coutant, PhD Senior Director, Lilly Research Labs

8:50 AM – 9:10 AM ***The Role of Dissolution in Development of Very Low and Low Risk Compounds***
Eva Karlsson, PhD Associate Principal Biopharmaceutics, Global Product Development, AstraZeneca

In vitro dissolution is a pivotal tool for risk assessment and quality control in product development, especially when it can be linked to in vivo exposure. However, for products with very low or low biopharmaceutics risk, where absorption is constrained by factors other than solubility or dissolution rate, routine dissolution testing may add little value. This presentation will discuss biopharmaceutics risk assessment focusing on very low and low risk products to exemplify how dissolution testing can contribute to drug development and when it potentially could be considered excessive.

9:10 AM – 9:30 AM ***From Solubility Challenges to In Vivo Predictability: Dissolution as a Low Risk Parameter in Oral Suspensions***
Biljana Janković, PhD Head of Pharmaceutical Research, Sandoz, Slovenia Development Centre

A slightly soluble drug substance formulated as an aqueous polymeric suspension shows rapid in vivo absorption with a very short T_{max}, indicating that solubility at the intended dose is sufficient and that dissolution is unlikely to be a critical parameter for in vivo performance. The presentation will highlight importance of selecting an appropriate dissolution method—either following principles for highly soluble drug substances or using a more complex method that also captures polymer related properties. Collaboration with regulatory agencies is encouraged to harmonize guidelines and align dissolution testing approaches for such formulations.

9:30 AM – 9:50 AM ***Fundamental Determinants for Justifying Low Biopharmaceutics Risk When Dissolution is Not Critical to Product Performance***
Tzuchi "Rob" Ju, PhD Director, AbbVie Inc.

This talk highlights when dissolution is not a key driver of performance and how API properties, formulation design, and release mechanism can support a low/very low biopharm risk rationale. It summarizes a focused evidence package (physicochemical characterization and fit-for-purpose in vitro testing) and uses two rapid-release case studies- one poorly soluble and one soluble- to illustrate how design parameters and release profiles can justify streamlined expectations for development and regulatory decisions.

9:50 AM – 10:10 AM ***Risk-Based Release Testing for Low-Risk Products: Disintegration Substitution and Clinically Justified Use of Standard Dissolution Method***
Hardikkumar Patel, PhD Senior Biopharmaceutics Assessor, DPQA XII, OPQA II, OPQ, CDER, FDA

Describe decision criteria and the minimal evidence package needed to (a) substitute disintegration for dissolution in low/very low-risk scenarios (including alternative assurances), and (b) use a standard, non-discriminating dissolution method when the overall risk narrative and clinical data support consistent PK performance—even if the API is not strictly "high solubility" by classic definitions.

10:10 AM – 10:15 AM ***Session 4 Summary***
Anitha Govada, PhD Senior Pharmaceutical Quality Assessor, DPQA VI, OPQA I, OPQ, CDER, FDA

10:15 AM – 10:30 AM ***Break***

Session 5: The Future of Dissolution - Beyond Quality Control
Session Leads: Dr. James Mann and Dr. Rebecca Moody

Scope: This forward-looking session explores the evolution toward predictive, patient-centric standards including Clinically Relevant Dissolution Specifications (CRDS) and the concept of "safe space" dissolution ranges where bioequivalence is assured. Discussions will cover the totality-of-evidence approach, the vision for harmonized global regulatory frameworks where scrutiny is proportional to biopharmaceutical risk, and how enhanced biopharmaceutics understanding represents a strategic investment yielding cost savings and development efficiency.

10:30 AM – 10:35 AM ***Speaker Introductions***
James Mann, MSci, PhD Principal Scientist, In Vitro Product Performance, AstraZeneca

10:35 AM – 11:00 AM ***Future of Dissolution Testing: Industry Perspective***
Johannes Moes, PharmD, PhD Scientific Director, Dissolution Sciences, J&J Innovative Medicine

The Future of Dissolution presentation will begin by examining the roles of QC focused and clinically relevant dissolution methods, and how these can be applied individually or combined to support quality control, regulatory decision making, and product lifecycle management. It will then discuss how exploratory "safe space" studies—using stressed materials, non-conforming batches, and controlled extremes—can build mechanistic understanding and demonstrate discriminative capability while remaining scientifically and regulatorily appropriate. The session will conclude by framing these concepts within the context of in vitro bioequivalence, aiming to establish guiding principles for robust, flexible, and future ready in vitro BE dissolution strategies.

11:00 AM – 11:15 AM ***Future of Dissolution Testing: Policy Perspective from FDA***
Kimberly Raines, PhD Associate Director of Science, OPPQ, OPQ, CDER, FDA

This talk will describe the future of dissolution testing as a natural progression within the current FDA policy for pharmaceutical quality, which can support more flexible, risk-based, and clinically relevant approaches. It will highlight how existing regulatory principles can be applied to advance dissolution methods that better reflect in vivo behavior and support product quality, clinical performance, and look forward to possible opportunities ahead.

11:15 AM – 11:25 AM ***Future of Dissolution Testing: Scientific Perspective from FDA***
Rebecca Moody, PhD Pharmaceutical Scientist, OPQA II, OPQ, CDER, FDA

This talk will define the evidence path for putting this policy direction into practice. It will focus on the assessment of dissolution methods that appropriately reflect in vivo behavior, including biopharmaceutics risk assessment, the totality of evidence supporting clinically relevant dissolution approaches, and practical considerations for regulatory submission packages.

11:25 AM – 11:50 AM ***From Established to Essential: How TIM Systems are Routinely Replacing In Vivo Assessments in Industry to Manage Biopharmaceutical Risk, and Accelerate Development***
Robert Schwabe, BS Senior Scientist, Boehringer Ingelheim Pharmaceuticals, Inc.

This presentation will discuss how TIM models, tiny-TIM and TIM-1, enable a physiologically relevant in vitro simulation of drug product performance in the upper human gastrointestinal tract under various intake conditions. The application of TIM systems related to formulation development and food effects have been established, whereas recent improvements have expanded to integrating data into in silico models to significantly improve clinical PK predictions and thereby inform decision-making in drug product development. Furthermore, the regulatory aspects and contribution to reducing animal experimentation (3R) will be discussed.

11:50 AM – 12:00 PM ***Session 5 Summary***
James Mann, MSci, PhD Principal Scientist, In Vitro Product Performance, AstraZeneca

12:00 PM – 1:00 PM ***Lunch Break***

Breakout Sessions: Low to Very Low Risk, Future

1:00 PM – 1:05 PM ***Transition to Breakout Session Rooms***

1:05 PM – 1:15 PM ***Introduction to Breakout Sessions Topic E and F***
Breakout Session by Moderators

1:15 PM – 2:15 PM ***Breakout Session E:*** Defining Low- and Very Low-Risk Products in Biopharmaceutics: A Framework Based on Physicochemical and Clinical Evidence

Breakout Session F: Strategizing the Future: Implementing Advanced, Risk-Based Control Frameworks

2:15 PM – 2:35 PM ***Break***

2:35 PM – 2:45 PM	***Breakout Session 3 Summary***	
	Robert Gaines, Jr., PharmD, MBA	Senior Director, Sciences and Regulatory Affairs, Association for Accessible Medicines
2:45 PM – 3:00 PM	***Closing Remarks***	
	CDR Geoffrey Wu, PhD, PMP, CPH	Office Director, OPQA I, OPQ, CDER, FDA