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 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***
Andreas Abend, PhD Senior Principal Scientist, Merck

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, 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 Senior Pharmaceutical Quality Assessor, 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***
Haritha Mandula, PhD Senior Pharmaceutical Quality Assessor, DPQA VI, OPQA I, OPQ, CDER, FDA
Rajesh Savkur, PhD Senior Assessor, 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 Founder, Technical Director, QPD Solutions, LLC

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

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 – 11:45 AM ***Development of a Dissolution Control Strategy and BE Safe-Space for a Solid-Dispersion Drug Product***
David Sperry, PhD Executive Director, 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.

11:45 AM – 11:50 AM ***Session 2 Summary***

11:50 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 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, 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 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, 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: 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 within a risk-based biopharmaceutics framework. These products are characterized by in vivo dissolution and systemic exposure that are influenced primarily by drug substance physicochemical properties and gastrointestinal (GI) physiological conditions rather than formulation-controlled release mechanisms. The discussion will focus on how mechanistic understanding of the interplay between drug product attributes and GI conditions can be integrated into the biopharmaceutics risk assessment process. Particular attention will be given to the role of biorelevant dissolution methods in supporting evaluation of factors that may influence in vivo pharmacokinetic performance. Case studies will be presented to illustrate how these approaches can inform regulatory assessment and improve understanding of product performance.

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

Breakout Sessions: Framework, High Risk, Medium Risk

2:15 PM – 2:25 PM ***Introduction to Breakout Sessions and Transition***
TBD Organization

2:25 PM – 3:25 PM ***Breakout Session A:***
Breakout Session B:

3:25 PM – 3:40 PM ***Break***

3:40 PM – 4:40 PM ***Breakout Session C:***
Breakout Session D:

4:40 PM – 4:55 PM ***Day 1 Closing Remarks***
Helena Engman, PhD Senior Principal Scientist, ADME Sciences, Seda Pharmaceutical Development Services

4:55 PM – 6:00 PM ***Networking Reception***

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***
Hardikkumar Patel, PhD Senior Assessor, DPQA XII, OPQA II, OPQ, CDER, FDA

8:50 AM – 9:10 AM ***The Role of Dissolution in Development of Very Low and Low Risk Compounds***
Eva Karlsson, PhD Associate Principal Scientist Biopharmaceutics, 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 Jankovic, PhD Head of Pharmaceutical Research, Lek, a Sandoz company

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

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 – 10:15 AM ***Risk-Based Release Testing for Low-Risk Products: Disintegration Substitution and Clinically Justified Use of Standard Dissolution Method***
Hardikkumar Patel, PhD Senior 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.

10:15 AM – 10:20 AM ***Session 4 Summary***

10:20 AM – 10:35 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.

10:35 AM – 10:40 AM ***Speaker Introductions***
James Mann, PhD Principal Scientist, In Vitro Product Performance, AstraZeneca

10:40 AM – 11:05 AM ***Future of Dissolution Testing: Industry Perspective***
Johannes Moes, PhD Scientific Director, 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.

11:05 AM – 11:30 AM ***Future of Dissolution Testing: Scientific and Policy Perspective from FDA***
Kimberly Raines, PhD Associate Director of Sciences, OPPQ, OPQ, CDER, FDA
Rebecca Moody, PhD Pharmaceutical Scientist, OPQA II, OPQ, CDER, FDA

This talk will explore the evolving landscape of dissolution testing, focusing on the strategic shift towards more flexible, risk-based, and clinically relevant methodologies. The presentation will underscore the need for developing dissolution methods that appropriately reflect in vivo behavior, thereby safeguarding product quality and clinical performance while streamlining regulatory processes. The discussion will cover the scientific rationale and policy framework for this evolution, including biopharmaceutics risk assessment, best practices for regulatory submissions, and strategies to accelerate regulatory convergence on clinically relevant standards.

11:30 AM – 11:55 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, PhD 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.

11:55 AM – 12:05 PM ***Session 5 Summary***

12:05 PM – 1:00 PM ***Lunch Break***

Breakout Sessions: Low to Very Low Risk, Future

1:00 PM – 1:10 PM ***Introduction to Breakout Sessions and Transition***
TBD TBD

1:10 PM – 2:10 PM ***Breakout Session E:***
Breakout Session F:

2:10 PM – 2:30 PM ***Breakout Session 3 Summary***

2:30 PM – 2:45 PM ***Closing Remarks***
Geoff Wu, PhD Director, OPQA I, OPQ, CDER, FDA