The Evolution of Biopharmaceutics: Risk Assessment and Clinical Relevance – Day 2

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Your Generics & Biosimilars Industry

Welcome to Day 2 – Building on a Strong Foundation

- Day 1 focused on advancing dissolution from QC → predictive, patient-centric science
- Strong alignment on the need for:
  - Science and risk-based approaches
  - Linking in vitro dissolution to in vivo performance
  - Regulatory and development integration across product lifecycle

- Dissolution as a decision-making tool … not just a test

Day 1 Highlights

- Session 1: Biopharmaceutics Risk Framework
  - Established a structured approach to identify, rank, and mitigate risk
  - Emphasis on predictive dissolution and clinical relevance
- Session 2: High-Risk Products (IVIVC/IVIVR)
  - Use of IVIVC/IVIVR and “BE Safe Spaces” to define performance boundaries
  - Integration of PK studies and modeling (physiologically-based biopharmaceutics modeling (PBBM)
- Session 3: Medium-Risk Products
  - Growing role of biorelevant dissolution methods
  - Opportunities to reduce BA/BE burden through science-based justification
- Breakout Sessions
  - Practical strategies to implement frameworks in real-world settings
  - Focus on risk differentiation and appropriate control strategies

Breakout Sessions – Objectives & Purpose

- Translate framework concepts into practical application
- Identify gaps, challenges, and areas needing clarification
- Align on scientific and regulatory expectations across risk categories
- Explore real-world implementation considerations (cost, complexity, feasibility)
- Promote dialogue across industry, FDA, and academia
- Support movement toward consistent, risk-based, and globally aligned approaches

Breakout A – From Concept to Implementation of a Risk Framework

- Theme: A strong framework exists but clarity, consistency, and practicality are critical for successful implementation.
- Need for clear definitions, terminology, and case studies
- Risk framework should reduce burden NOT add complexity or subjectivity
- Concerns on:
  - Medium risk: potential increased workload (e.g., dual methods)
  - High risk: disconnect between risk level and regulatory expectations
- Strong emphasis on global harmonization and consistency across agencies

Breakout B – High-Risk Products & Clinical Relevance

- Theme: Scientific complexity requires robust tools—but current methods and models still have limitations.
- High-risk products driven by complex drug–formulation–physiology interactions
- Challenges in:
  - Developing IVIVC/IVIVR
  - Predicting performance a priori
- Mechanistic modeling and biopredictive dissolution are valuable but:
  - Require significant validation
  - May not fully capture real-world behavior
- Need for fit-for-purpose, scientifically justified methods vs. default approaches

Breakout C – Defining Medium Risk

- Theme: Medium risk is not a category rather it is a continuum defined by complexity, interactions, and evolving evidence.
- Medium risk emerges from interplay of API, formulation, and GI physiology
- No single factor—requires multivariate, mechanistic understanding
- Key discussions:
  - Role of formulation technologies (enhancing vs. controlling release)
  - Importance of measurement approaches and modeling strategies
- Strong support for:
  - Dynamic, evidence-based risk classification
  - Potential to downgrade risk as data accumulates
- Need for clearer expectations, thresholds, and case studies

Breakout D – Control Strategy for Medium Risk

- Theme: Control strategies must balance scientific rigor with practical feasibility.
- Dissolution remains essential, even when upstream controls are strong
- Debate on:
  - Biorelevant vs. QC dissolution methods
  - Value of “two-method” approaches
- Decisions should be based on totality of evidence
- Key challenges:
  - Cost and operational complexity
  - Implementation barriers for advanced methods
- Strong call for clear, harmonized regulatory expectations

Key Takeaways – Day 1

- Clarity and Definitions are not only needed but foundational
  - Need for clear terminology, expectations, and examples to enable implementation
- Risk-Based ≠ More Burden
  - Framework must reduce subjectivity and complexity, not increase it
- Science is Advancing Faster than Frameworks
  - Strong interest in modeling, biopredictive dissolution, and mechanistic approaches
  - But validation, consistency, and regulatory acceptance remain challenges
- Medium Risk = The Biggest Opportunity (and Challenge)
  - Requires flexible, evidence-based, and dynamic classification
  - Currently lacks clear boundaries and expectations
- Global Harmonization is Critical
  - Consistency across Health Authorities is essential for efficient development and lifecycle management
- Implementation Must Be Practical
  - Consider cost, feasibility, and operational complexity alongside scientific rigor

Thank you !!

Merci · Gracias · Danke · Grazie · Obrigado

谢谢 · ありがとうございます · 감사합니다 · धन्यवाद

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Спасибо · Terima Kasih