Future of Dissolution Testing: FDA Policy Perspective

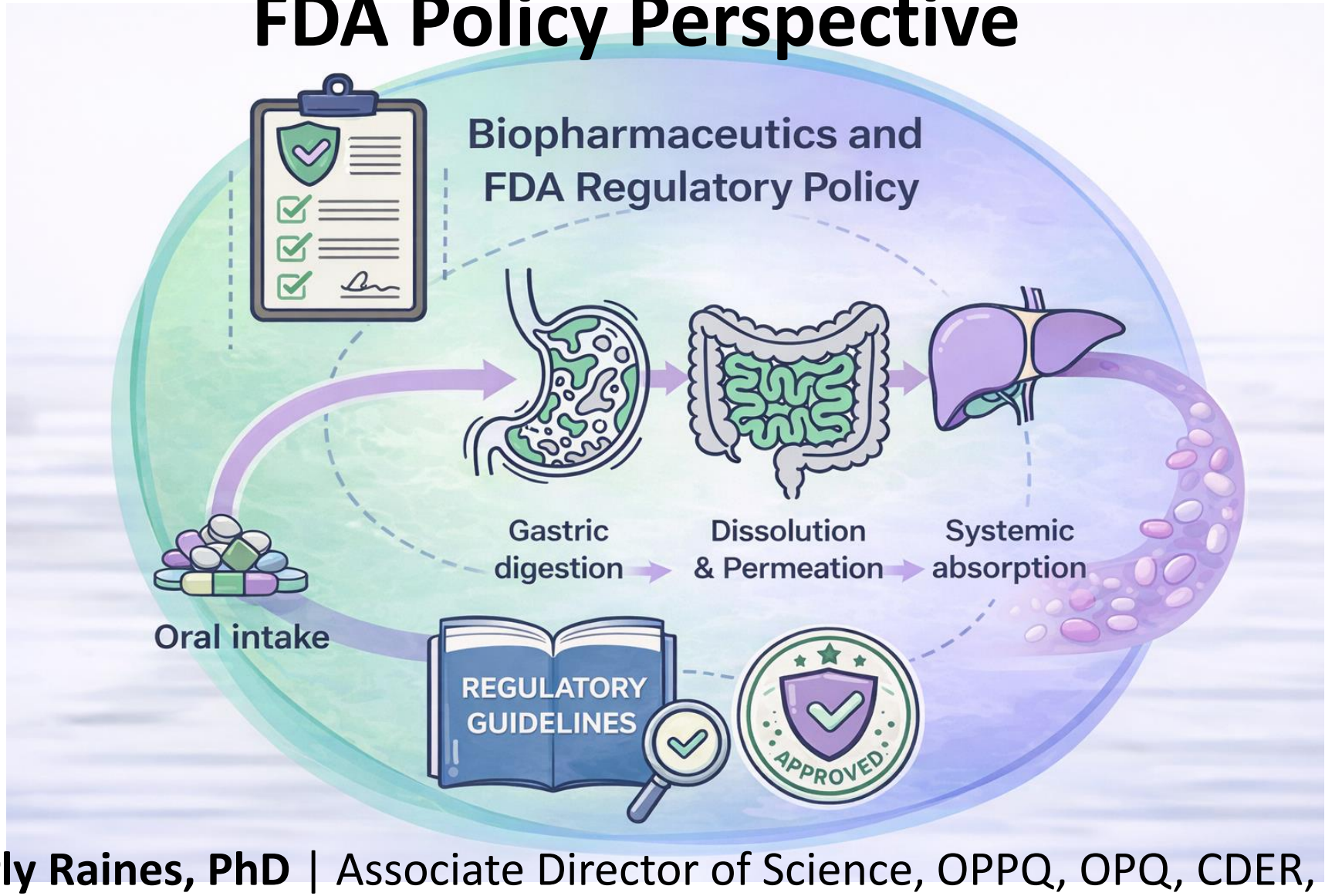

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Figure adapted from: Optimizing Oral Drug Delivery: Unlocking Bioavailability through Simultaneous Dissolution and Permeation Studies

Disclaimer

This presentation reflects the view of the presenter and should not be construed to represent FDA's views or policies.

The Future of QC Dissolution Testing

The future is not replacing QC dissolution with a single universal “clinically relevant” test. The future is using the right dissolution approach for the right regulatory question, with the level of clinical linkage proportional to biopharmaceutic risk and decision consequence.

Evaluation approach → Right dissolution question → Decision consequences proportional

This understanding provides rationale for flexibility that is scientifically based because when dissolution is known not to be the rate-limiting step in absorption, additional complex evaluation often doesn’t provide added insight or knowledge for lifecycle management.

FDA Regulatory Policy

Operating Principle:

- The FDA's regulatory framework is a **science-based system grounded in federal law**, primarily the *Federal Food, Drug, and Cosmetic (FD&C) Act*.
- It is designed to ensure the **safety, effectiveness, and security** of drugs, medical devices, and food products.
- The framework applies a **risk-based approach** across the product lifecycle, including:
  - **Pre-market evaluation and approval**
  - **Manufacturing quality standards (CGMP)**
  - **Post-market surveillance and monitoring**
- Decision-making is driven by the **continuous interaction of law, science, and risk assessment**.

Why this conversation matters

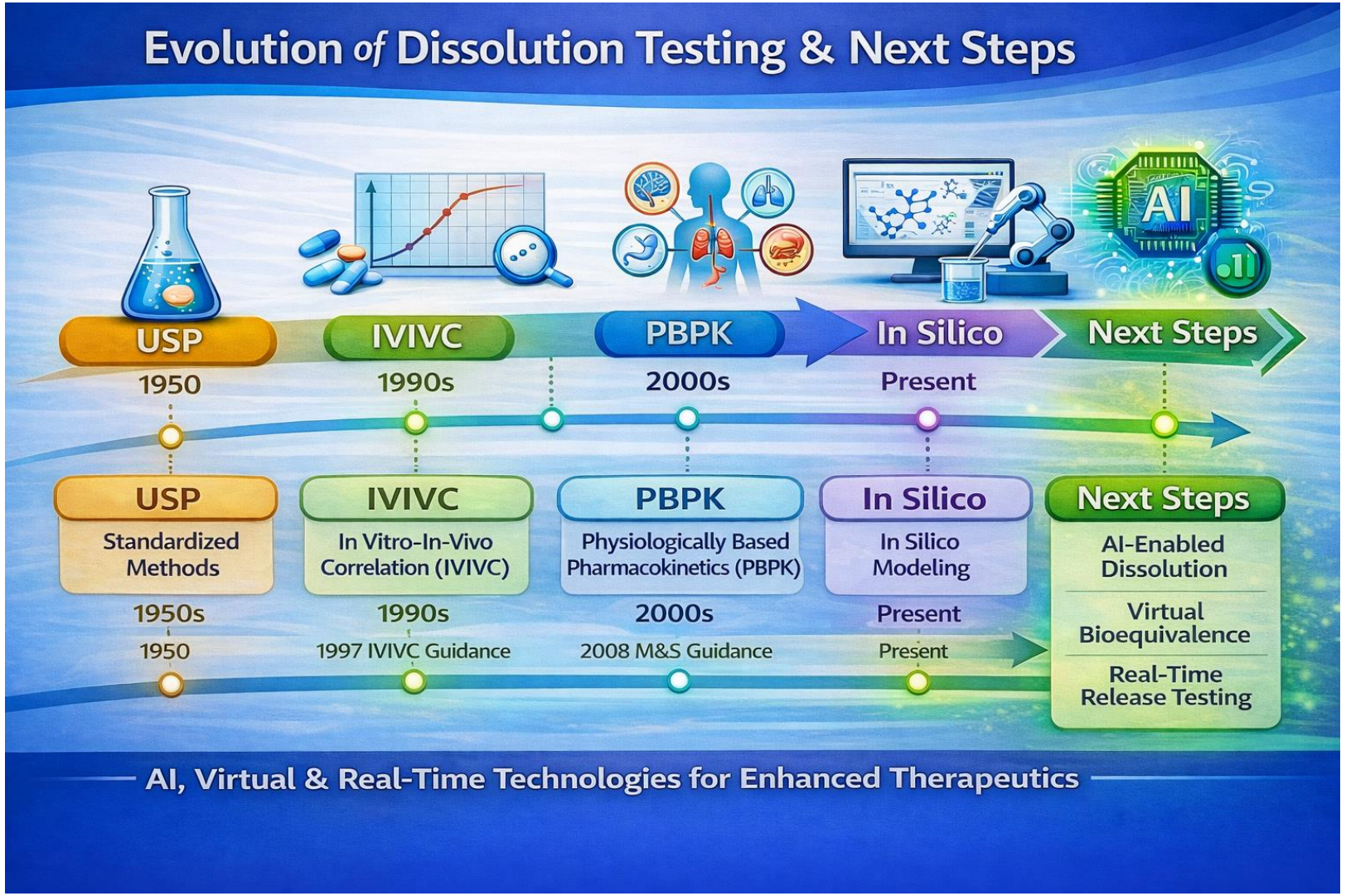
Dissolution remains a standard expectation for many solid oral products, but the **regulatory value** of the test is product-dependent.

For some products, conventional QC dissolution is sufficient to assure performance, but often not clinically relevant and potentially redundant to other quality measures.

For others, a purely QC-centric method can be scientifically disconnected from the real decision at hand: approval, additional-strength bridging, postapproval change, or investigation of outlier performance.

Dissolution should be assessed by its fitness for the decision it is asked to support

Dissolution is Evolving and FDA Policy is Adapting



FDA Dissolution Guidance Overview

• Key Published Guidance:

- ✓ **ICH Q6A** on specifications and role of dissolution in solid oral dosage forms.
- ✓ FDA's **1997 IR dissolution** guidance.
- ✓ FDA's **1997 ER IVIVC** guidance.
- ✓ FDA's **2018 high-solubility IR guidance**.
- ✓ ICH **Q8(R2), Q9(R1), Q10, Q12, and Q14**.
- ✓ ICH/FDA **M9 and M13**.

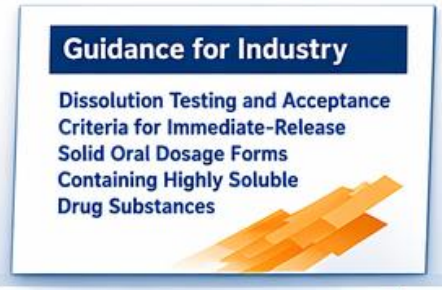
• Established Risk-based Framework:

- ✓ **Q6A** distinguishes **IR single-point vs. MR multi-point** expectations and notes that in some cases dissolution can be replaced by disintegration.
- ✓ **ER IVIVC guidance** provides recommendations for using **IVIVC** to set **dissolution** specifications and, in some cases, as a **surrogate for in vivo BE**.
- ✓ The Use of **Physiologically Based Pharmacokinetic Analyses – Biopharmaceutics Applications for Oral** Drug Product Development, Manufacturing Changes, and Controls GUI currently outlines strategy for design and use of modeling and simulation.

Guidance based on Lifecycle
Risk-Based Thinking

Dissolution Testing for Immediate-Release High Solubility Drugs

Provides acceptance criteria and recommendations for immediate-release products containing highly soluble drug substances using standard release tests.



Biopharmaceutics Classification System (BCS)-ICH M9

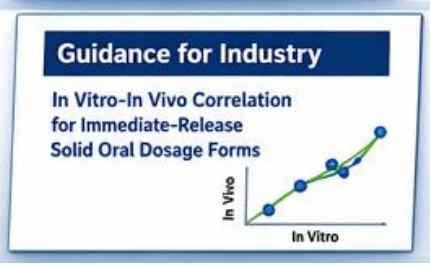
BCS framework combined with dissolution testing to justify biowaiver for highly soluble and permeable drugs in immediate-release formulations.

Scale-Up and Post-Approval Changes (SUPAC)

Evaluates dissolution testing to assess the impact of manufacturing changes on product quality and performance.

In Vitro-In-Vivo Correlation (IVIVC)

Establishing an IVIVC can reduce the need for in vivo studies for certain products and changes.



Regulatory Flexibility
Increasing reliance on PBPK and M&S

- Supports biowaivers
- Supports formulation bridging
- Predicts absorption
- Informs specifications

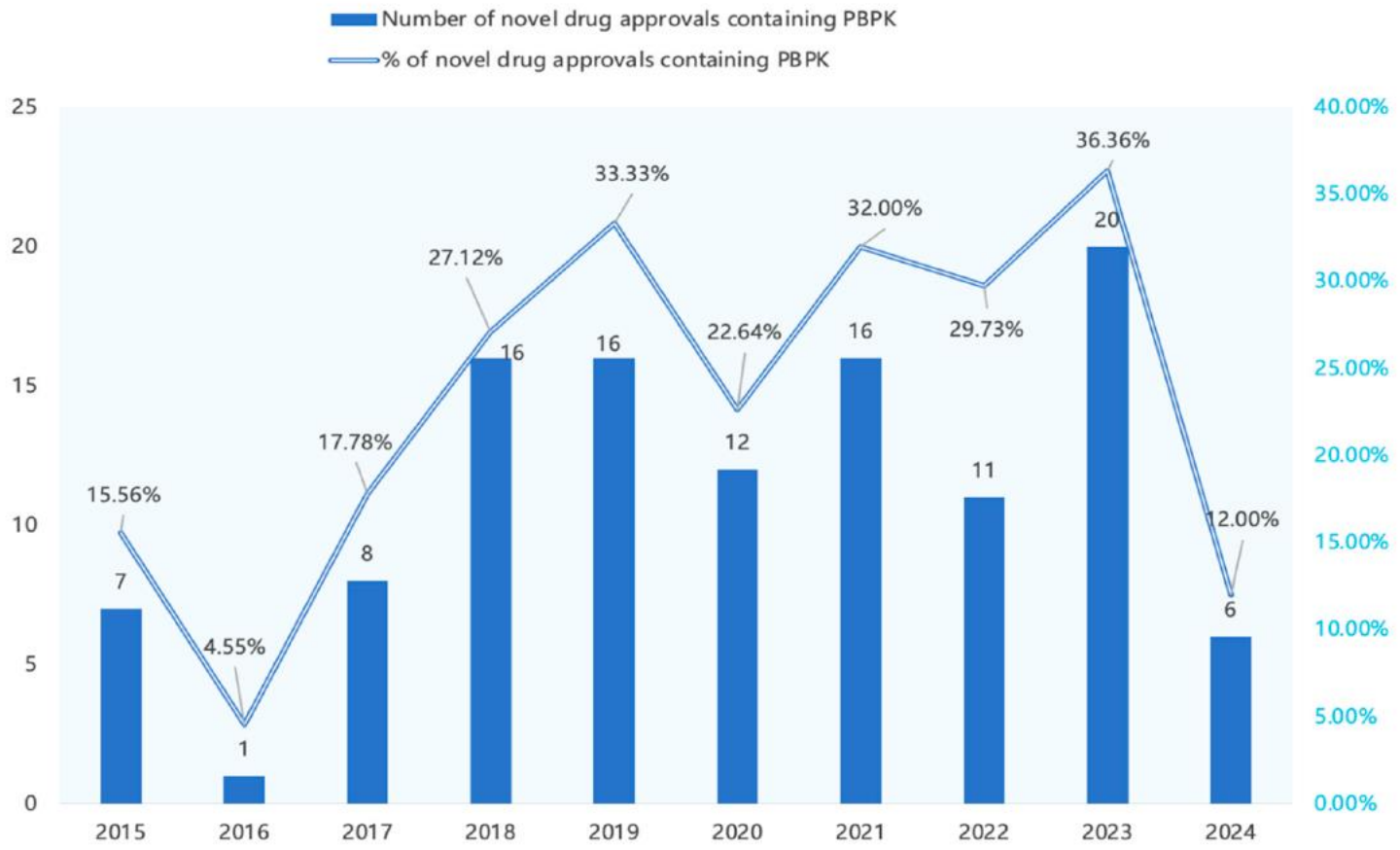


Figure 1. PBPK Model Use in FDA-Approved New Drugs (2015–2024).

Pharmaceutics **2025**, *17*(11), 1413; https://doi.org/10.3390/pharmaceutics17111413

Forward-Thinking Policy Perspective for the Future of Dissolution

Current Challenges

- Inconsistent Results
- Time-Consuming Methods
- Lack of Physiological Relevance

Proposed Solutions

- Advanced Dissolution Models
- Biorelevant Testing
- Harmonized Standards

Technology Advances

- Automated Systems
- In Situ Analysis
- Analytical Innovations

Regulatory Roadmap

- Guideline Updates
- Risk-Based Approaches
- Global Alignment
- Training & Education

Ensuring Drug Quality & Patient Safety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