U.S. FOOD & DRUG ADMINISTRATION

Summary of Session 4: Low-Risk and Very Low Risk Products

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Public Workshop: The Evolution of Biopharmaceutics: Risk Assessment and Clinical Relevance
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Disclaimer

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

Session- 4 Presentations Recap

The biopharmaceutics risk assessment framework: Is dissolution testing truly necessary for very low risk and low risk compounds?

Dissolution testing should be fit-for-purpose, calibrated to actual drivers of in vivo performance, not applied uniformly across all formulation types

Routine dissolution testing may be an **excessive regulatory and development burden.** PBBM for **expanding biowaivers beyond BCS 1 and 3.**

Case study of an aqueous polymeric suspension product. the importance of **selecting an appropriate dissolution method (standard vs complex).**

The concept of a focused evidence-based data package as a **streamlined alternative to extensive dissolution method development**

Disintegration test or Standard Dissolution Method when clinical PK data **supports** consistent performance.

Key Takeaways from Session 4

Rethink Dissolution for Very Low and Low-Risk Compounds

A comprehensive risk assessment should be the foundation of that rethinking.

Very low-risk products may qualify for dissolution testing waivers

Disintegration in lieu of dissolution

Supporting clinical/PK data justification

Standard dissolution methods vs. complex methods for in vivo predictability

A shift from "rule-based" to "risk-based" testing.

Conclusion

LOW RISK ≠ NO STANDARDS FOR REGULATORY COMPLIANCE

QUALITY CONTROL TO ENSURE CONSISTENT PRODUCT QUALITY THROUGHOUT THE PRODUCT LIFECYCLE

BASELINE SAFETY AND PERFORMANCE STANDARDS WHILE MAINTAINING HIGH QUALITY AND CONSISTENCY.

Breakout Session E

Disintegration in lieu of dissolution

Biopharmaceutics risk classification of Low- and Very Low-risk products

Simple Dissolution tests for Low-risk products

Fit-for-purpose dissolution methods

Justification beyond BCS for low risk and very risk - Global regulatory alignment

Thank You!

Session 5 starts after a short break.

Breakout Session E

Group	Moderator (Regulatory)	Moderator (Industry)	Scribe
Group E-1 (Room 1032)	Tapash Ghosh	Eva Karlsson	Moshe Honick
Group E-2 (Room 2032)	Rushikesh Sable	Carrie Coutant	Arindom Pal
Group E-3 (Room 2052)	Rajesh Savkur	Susan Ewing	Jiaher (Jacob) Tian
Group E-4 (Ballroom)	Anitha Govada	Tzuchi “Rob” Ju	Nadia Ahmed

Breakout Session E: Questions

1. When is it scientifically justified to use disintegration in lieu of dissolution for Low- or Very Low-risk products?

- What product attributes support Very Low vs. Low-risk categorization?
- Is specific product development testing data needed to justify the risk level?
- What level/type of disintegration–dissolution relationship is sufficient to support the transition from dissolution to disintegration?
- How does this align with ICH Q6A principles?

Breakout Session E: Questions

2. When dissolution is required for QC of Low-Risk products, what should a fit-for-purpose method demonstrate?

- Is the standard method listed in the FDA guidance sufficient or acceptable?
- Is discriminating ability even relevant for a fit-for-purpose method?
- How to balance development of dissolution method for QC vs. scientifically justified/clinical or bio-relevant methods?
- How critical is acceptance criterion time point for low-risk products, with rapid drug release.
- Should there be flexibility set acceptance criterion at other timepoints based on Tmax (30 mins vs 15 min vs 45 mins)? What level of justification should be provided for changes in AC (%drug release and time point).

Breakout Session E: Questions

3. Beyond BCS: Evidence needed to justify Low or Very Low risk and how to improve global regulatory alignment?

- How to justify Low risk outside “high solubility”?
- What evidence is essential vs. supportive?
- What would improve consistency across agencies?

Breakout Session E: Questions

4. What should a practical framework look like for the initial biopharmaceutics risk classification of Low- and Very Low-risk products?

- Key physicochemical factors?
- Common Pitfalls and Best Practices for Dissolution Method Development
- Impact of formulation, process and DOE on product development?
- Consideration of Clinical/PK/in silico data for determining the risk level?
- When can QC be streamlined to cover most drugs using standardized method and when should this be more product-specific decision?