U.S. FOOD & DRUG ADMINISTRATION

Public Workshop: New Insights for Product Development and Bioequivalence Assessments of Generic Orally Inhaled and Nasal Drug Products (OINDPs)

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Session 1: Predictive Dissolution Methods for OINDPs

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Dissolution Methods for OINDPs

- Dissolution studies are routinely used for characterization of oral drug products, as both quality control and bio-predictive tools
- Predictive in vitro drug dissolution tests may provide a link between regional drug deposition and local/systemic pharmacokinetics for OINDPs containing poorly soluble drugs
- Bio-predictive dissolution tests may provide insight about potential in vivo performance variability of RLD and generic test products, and reduce the likelihood of comparative clinical study failures during BE determinations

But…

- Unlike for oral products, limited information on development of dissolution methods for OINDPs is available in the literature
- Development and validation of a bio-predictive dissolution method for OINDPs can be challenging

Key Challenges with Development of Dissolution Methods for OINDPs

- Sample collection
- Method for transferring collected samples to dissolution apparatus
- Sink condition vs. low volume physiologically relevant conditions
- Number of dissolution media
- Validation/bio-predictability
- Acceptance criteria
- Standardization of the method

Development of Dissolution Test for OINDPs

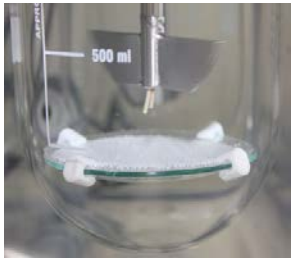
Sample Collection
- Canister
- Spray
- Blister
- Impactor
- Dosage unit sampling apparatus

Apparatus
- USP
- Flow-through system
- Diffusion-controlled apparatus

Medium
- Buffered saline
- Simulated lung fluid
- Artificial nasal fluid
- Purified lung fluid
- Simulated GI fluid

Method Validation
- Predictability
- Discriminatory power
- Both

BE Assessment
- Dissolution rate constant
- Entire profile
- Model-based comparison



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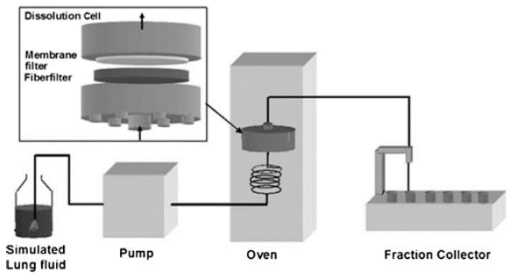

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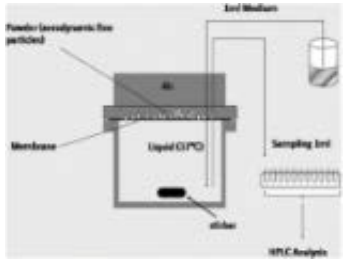

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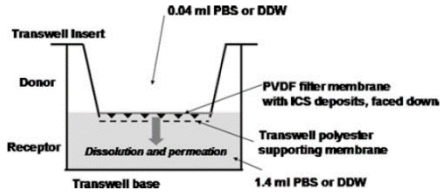

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Focus of the Session

- Different Dissolution Methods for characterization of OINDPs
  - Method development/optimization
  - Validation
  - Application/case examples
  - Pros and cons of individual methods

Presentation 1: Development of an Optimized Dissolution Test System for OINDPs– Guenther Hochhaus, PhD (University of Florida)

Presentation 2: Discriminative *In Vitro* Dissolution Testing for Orally Inhaled Drug Products: Transwell-based System – Masahiro Sakagami, PhD (VCU)

Presentation 3: Dissolution and Beyond: The Use of Advanced Characterization Tools for Demonstrating Pharmaceutical Equivalence of Orally Inhaled Drug Products - Robert Price, PhD (University of Bath)

Panel Discussion - Role of Dissolution in Development and Bioequivalence Assessment of Orally Inhaled Drug Products