Breakouts version: May 22, 2023

M-CERSI Workshop on Drug Dissolution in Oral Drug Absorption

May 23-24 2023 in Pharmacy Hall at the University of Maryland Baltimore, in Baltimore, MD.

www.pharmacy.umaryland.edu/dissolution2023

Each breakout is 1 hour in duration and expected to involve 15-25 participants. A breakout is not intended to be a lecture, but rather a discussion where attendees share experiences and best practices and identify current challenges. A question for each breakout is: What public/pre-competitive research, policy update, or collaborative effort is needed to bring the area forward?

Day 1: Tue, May 23 2023

3:00 – 4:00 p.m. Breakout Sessions A

Session A1: RTRT to replace in vitro dissolution

Room: PH N306

Topic Question: What are the best real-time release testing (RTRT) practices to replace in vitro dissolution testing?

Additional questions and talking points:

1. Benefit of RTRT?
2. Best practice of RTRT model development
3. Model validation
4. Model maintenance over product lifecycle?
5. Model transfer?
6. Reg. burden? If any
7. Special sampling requirement?
8. Modeling profile vs. single point?
9. Challenges and future opportunities

Leads: Hanlin Li (Vertex) / Haritha Mandula (FDA)

Scribes: Rebecca Moody (FDA)

Session A2: Drug dissolution from nano-formulations

Room: PH N310

Topic Question: What in vitro dissolution and dissolution/permeation methods have been most useful for nano-formulations?

Leads: David Curran (GSK) / Anitha Govada (FDA)

Scribes: Lucas Attia (MIT) and Rutu Valapil (U of Maryland)

Session A3: Non-compendial methods

Room: PH N314

Topic Question: Definition of non-compendial methods? Under what conditions has any particular non-compendial method been helpful, and why? Are such non-compendial methods complementary or potential replacements for compendial methods?

Leads: Kerstin Schaefer (Boehringer-Ingelheim) / Hansong Chen (FDA)

Scribes: Kalpana Paudel (FDA) and Johanna Milsmann (Boehringer-Ingelheim)

Session A4: Drug dissolution from lipid-based formulations

Room: PH N301A

Topic Question: What in vitro dissolution methods have been most useful for lipid-based formulations?

Leads: Anette Mullertz (University of Copenhagen) / Leah Falade (FDA)

Scribes: Payal Agarwal (FDA) and Bryan Ericksen (FDA)

Day 2: Wed, May 24 2023

1:00 – 2:00 p.m. **Breakout Sessions B**

Session B1: Drug dissolution from co-crystals

Room: PH N306

Topic Question: What in vitro dissolution and dissolution/permeation methods have been most useful for co-crystals?

Leads: Serajuddin Abu (St Johns) / Alaadin Alayoubi (FDA)

Scribe: Yuly Chiang Yu (U of Maryland)

Session B2: Ionizable drugs or excipients: buffer capacity considerations

Room: PH N310

Topic Questions:

1. At what stage during the product development process are dissolution medium modified to take into consideration ionizable drugs and excipients?

2. What different buffer systems are investigated for ionizable drugs and excipients?

3. Are buffer systems used for dissolution testing a part of quality control dissolution method or are they used exclusively for product development/research activities?

4. What are the major gaps in developing leveraging in silico tools to predict performance of ionizable drugs and drug products with ionizable excipients?

Leads: Rohit Jaini (Pfizer) / Parnali Chatterjee (FDA)

Scribe: Huong Moldthan (FDA)

Session B3: Non-compendial testing for ASDs from industry and regulatory perspective

Room: PH N314

Topic Question: For ASDs, what non-USP methods are most useful compared to regulatory dissolution methods?

Leads: Lynne Taylor (Purdue) / Andre Hermans (Merck) / Rajesh Savkur (FDA)

Scribe: Carrie Coutant (Lilly)

Day 2: Wed, May 24 2023

2:15 – 3:15 p.m. **Breakout Sessions C**

Session C1: In vitro approaches to interpret/predict food effects

Room: PH N306

Topic Question: What in vitro dissolution or dissolution/permeation methods have been shown to anticipate positive, negative, or no food effect?

Driving Discussion Thoughts:

- Known physiological effects of food
- Examples of these effects influencing API and/or dosage forms
- Prediction: which information is needed?
- Experimental approaches to capture the effects
- Examples where all in vitro approaches failed to capture the food effect (if any)

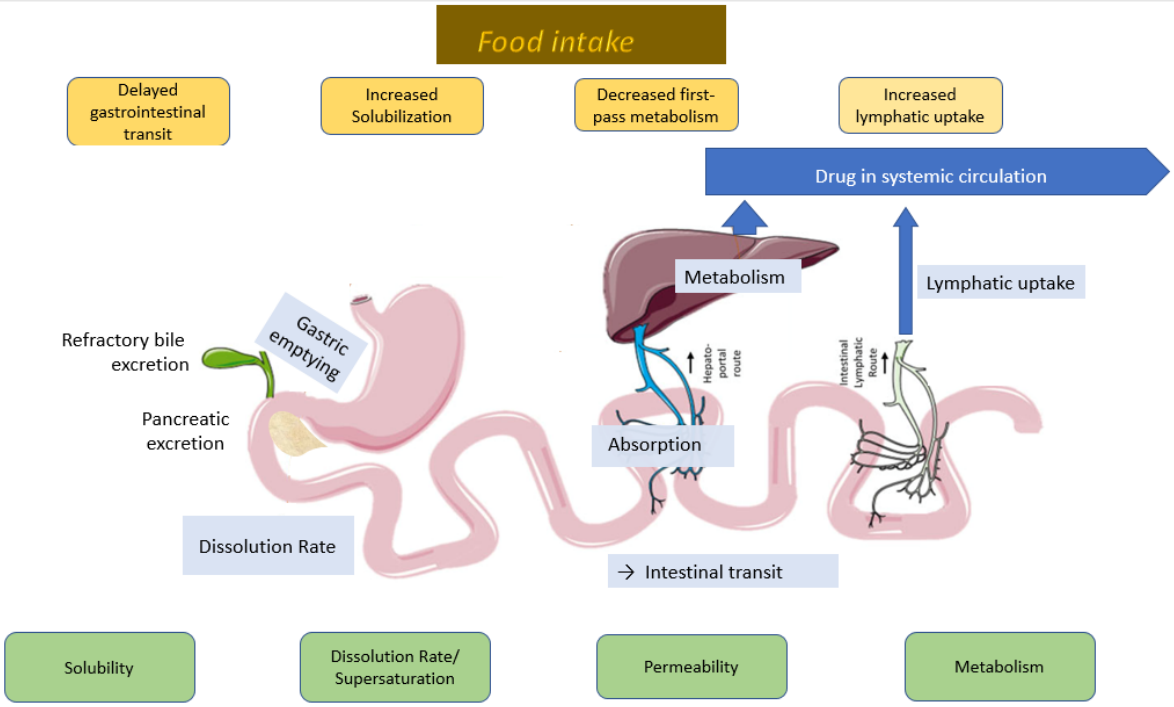

Figure inspired by O´Shea et al., JPP, 2022

Lead - Martin Brandl (U of Southern Denmark) / Annette Bauer-Brandl (U of Southern Denmark) / Kimberly Raines (FDA)

Scribes: Rajesh Savkur (FDA) and Roshni Patel (U of Maryland)

Session C2: Drug dissolution from amorphous solid dispersions

Room: PH N310

Topic Question: What basic and applied laboratory methods provide the best insight into drug dissolution from amorphous solid dispersions?

Topic 1: How are biorelevant dissolution studies best designed?

- Sink vs non-sink conditions; Sink index; Media selection (pH, additional components); Single stage or two stage

Topic 2: How are formulations best designed to de-risk bioperformance?

- Drug loading; Drug-polymer interactions; Polymer selection; Glass transition temperature

Topic 3: How can in vitro dissolution be used in risk assessment?

- Detection of crystallinity by dissolution and/or orthogonal techniques; Inform about potential significance of crystallinity on performance; Characterization tools; Biopharmaceutics modeling

Leads: Dana Moseson (Pfizer) / Debasis Ghosh (FDA)

Scribe: Ana Luisa Coutinho (U of Maryland)

Session C3: Non-USP methods versus regulatory methods: biopharmaceutic risk assessment

Room: PH N314

Topic Questions:

How do you initiate developing a dissolution method for your product? 505 (b)(1) vs 505 (b)(2) vs ANDA products?

What leads you to pursue or not pursue non-USP method as your ultimate regulatory method?

Have you filed a non-USP method and gained an approval from regulatory agencies worldwide?

What can be the potential risk/benefits and technical challenges in adopting and transferring a non-compendial method to commercial testing sites, especially for a non-NME?

Leads: Yi Gao (AbbVie) / Tapash Ghosh (FDA)

Scribes: Elizabeth Gray (FDA) and Ruiqiong Guo (Takeda)