Break out information for:

M-CERSI workshop: Drug Permeability: Best Practices for BCS-based Biowaivers

December 6, 2021

Two sequential break out sessions span from 2pm – 4pm ET. Each session is 55 minutes in duration and repeated at 3pm with different workshop attendees. All attendees can participate in two breakout sessions, i.e. at 2pm and 3pm. Participants will be able to indicate their prefer for two break to session when registering.

Breakout Session #1: In vitro and in silico intestinal permeability methods

Co-Leads: Donna Volpe, FDA and Yu Chung Tsang, Apotex

Objectives: Identify permeability assessment methods (e.g., cell lines other than Caco-2, such as primary cells, co-cultures, 3D systems [organoids, microfluidics [2D and 3D], non-cellular methods [PAMPA], and computational permeability approaches), including how to validate methods (e.g., comparison to Caco-2 data or human %Fa)

• What other cell lines besides Caco-2 have been used to measure passive and active intestinal drug permeability that can designate permeability class?

• What non-cellular models are available to measure passive intestinal drug permeability that can designate permeability class?

• What in silico models predict passive intestinal drug permeability and can designate permeability class? Should the models be based upon Caco-2 results or human %Fa?

• How should the different models (cellular, non-cellular, in silico) be validated to ensure accurate prediction of high permeability?

Breakout Session #2: Excipient effects on permeability, do we need to be concerned?

Co-Leads: James Polli, University of Maryland and Pablo Gonzalez, Biopharmaceutical Evaluation Center, Chile

Objective: Identify excipients that do not need to be Q1 and/or Q2 in various situations, including any limits on excipient amounts

• What common excipients are known to modulate the human in vivo permeability of highly permeable drugs? What common excipients appear to perhaps modulate the human in vivo permeability of highly permeable drugs, from human in vivo studies?

• In spite of use in human in vivo studies, what common excipients are known to modulate the permeability of high or low permeability drugs, and merit caution in human in vivo studies? How were they determined (in vitro and/or in vivo)?

• What non-common excipients are known to modulate the human in vivo permeability of high or low permeability drugs, from human in vivo studies? What non-common excipients appear to perhaps modulate the human in vivo permeability of high or low permeability drugs, from human in vivo studies?

• For any of the above questions, should there be limits to excipient quantities in the drug product?

Breakout Session #3: Use of label and literature data to designate permeability class

Co-Leads: Shereeni Veerasingham, HC and Susana Almeida, Medicines for Europe

Objective: Identify label and literature data types that can serve as primary data to classify permeability as high, and requirements to be met.

• What in vivo data derived from published literature may be acceptable to classify a drug as highly permeable? (e.g., absolute bioavailability, mass balance, %Fa)

• What are acceptable sources of in vivo data reports for this purpose? (e.g., product labels, regulatory review reports, peer-reviewed articles)

• What details do these reports require for the data to be considered acceptable? (e.g., reference standards)

• Are published reports on Caco-2 cell permeability assays acceptable? (e.g., regulatory review reports, peer-reviewed articles)