Welcome and Opening Remarks

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Dec 6 2021

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

Biopharmaceutics Classification System (BCS)

- BCS is a well-established scientific framework based on solubility and permeability of the drug substance, plus dissolution of the drug product
- Provides assurance of in vivo bioequivalence based on extensive in vitro comparative characterization
- BCS provides a pathway to avoid unnecessary human studies
- BCS was finalized in 2019 as the ICH M9 guidance
- The most difficult criterion to establish is that the drug substance is highly permeable
  - Mass-balance or absolute bioavailability, or extensive in vitro cell permeability data using a properly validated system
- To discuss the industry, academic and regulatory experience in generating and evaluating permeability data which will further facilitate implementation of BCS and efficient development of high-quality drug products globally.

Items on M-CERSI website

- Agenda
- Biographies
- Breakout session information

- https://cersi.umd.edu/event/16683/drug-permeability-best-practices-for-bcs-based-biowaivers

- Within ~3 weeks, speaker slides will be available, along with recordings from the 8:30 AM-2:00 PM and 4:05 PM-4:20 PM “main workshop”

Breakout session information

- Breakout Session #1: In vitro and in silico intestinal permeability methods
  - Identify permeability assessment methods other than Caco-2 and how to validate methods
- Breakout Session #2: Excipient effects on permeability, do we need to be concerned?
  - Identify excipients that do not need to be Q1 and/or Q2 in various situations, including any limits on excipient amounts.
- Breakout Session #3: Use of label and literature data to designate permeability class
  - Identify label and literature data types that can serve as primary data to classify permeability as high, and requirements to be met.

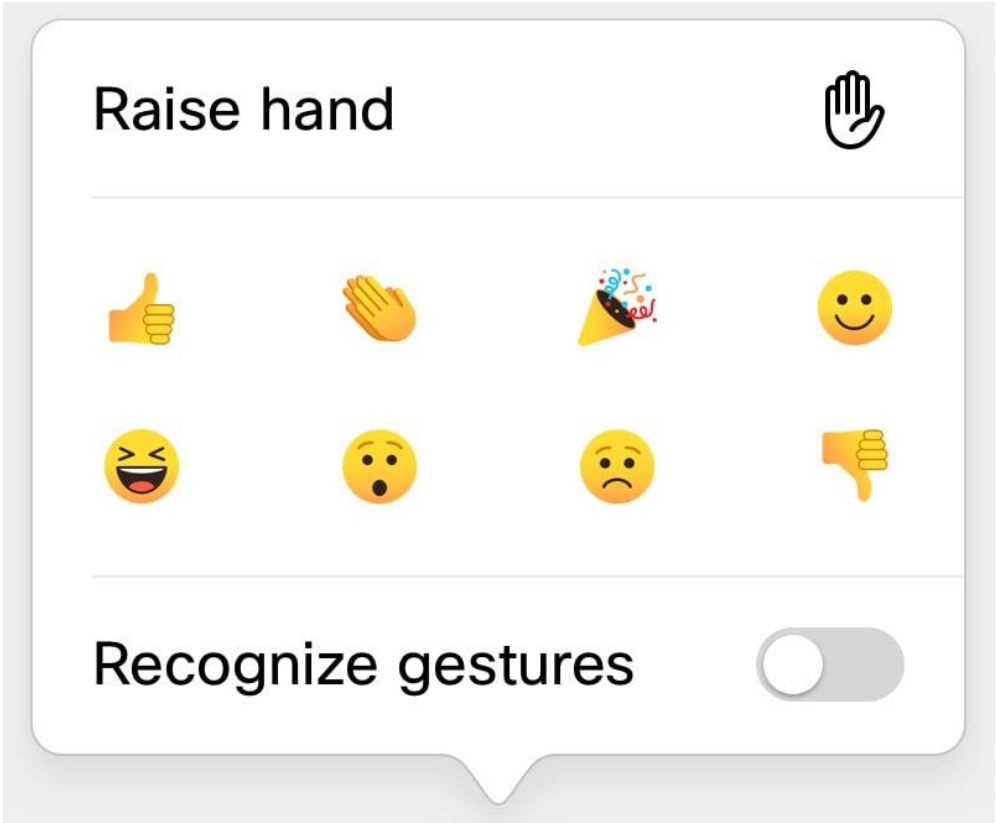
Webex logistics

- “Main workshop” URL link
  - 8:30am - 2pm
  - 4:05 - 4:20pm
  - Please enter questions into Chat at anytime for panel discussion
- Separate URL link for 2pm breakout session
  - 2-3pm
  - Please “raise your hand” to be recognized (to speak); enter questions into Chat
- Separate URL link for 3pm breakout session
  - 3-4pm
  - Please “raise your hand” to be recognized (to speak); enter questions into Chat

- aanonsen@umd.edu

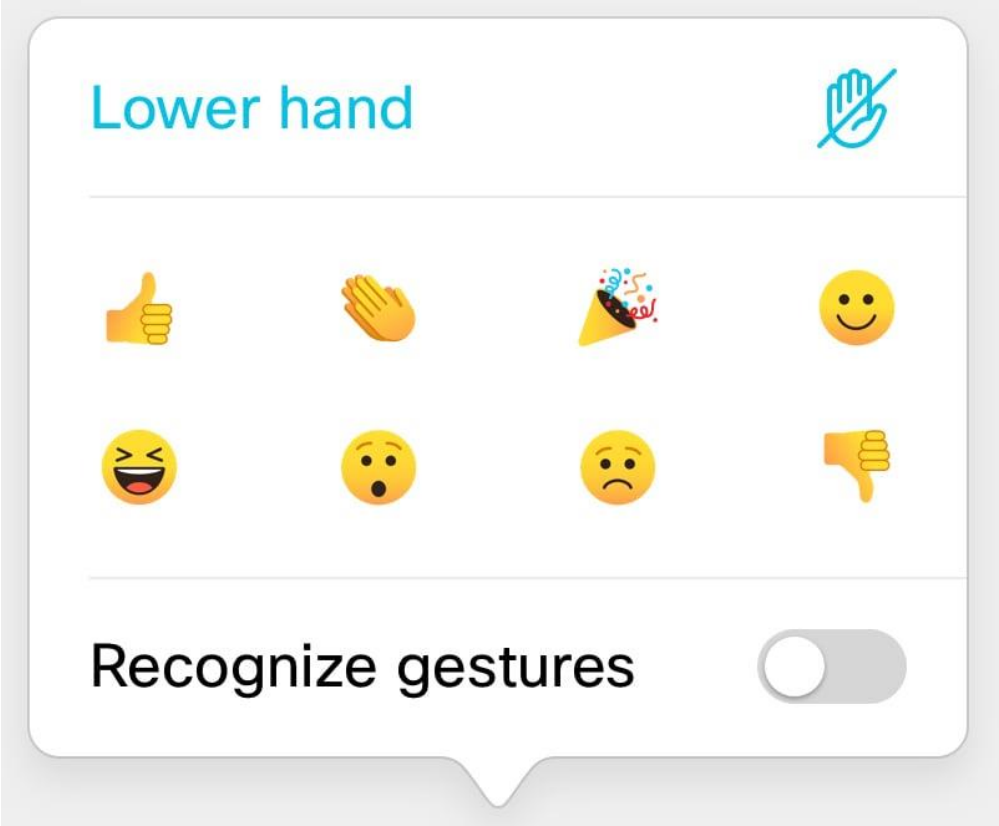
Breakout sessions:
How to raise hand in Webex?

- At the bottom center of Webex, select the **React** button,  , and tap **Raise hand**. Reaction button also available via **More** button  .

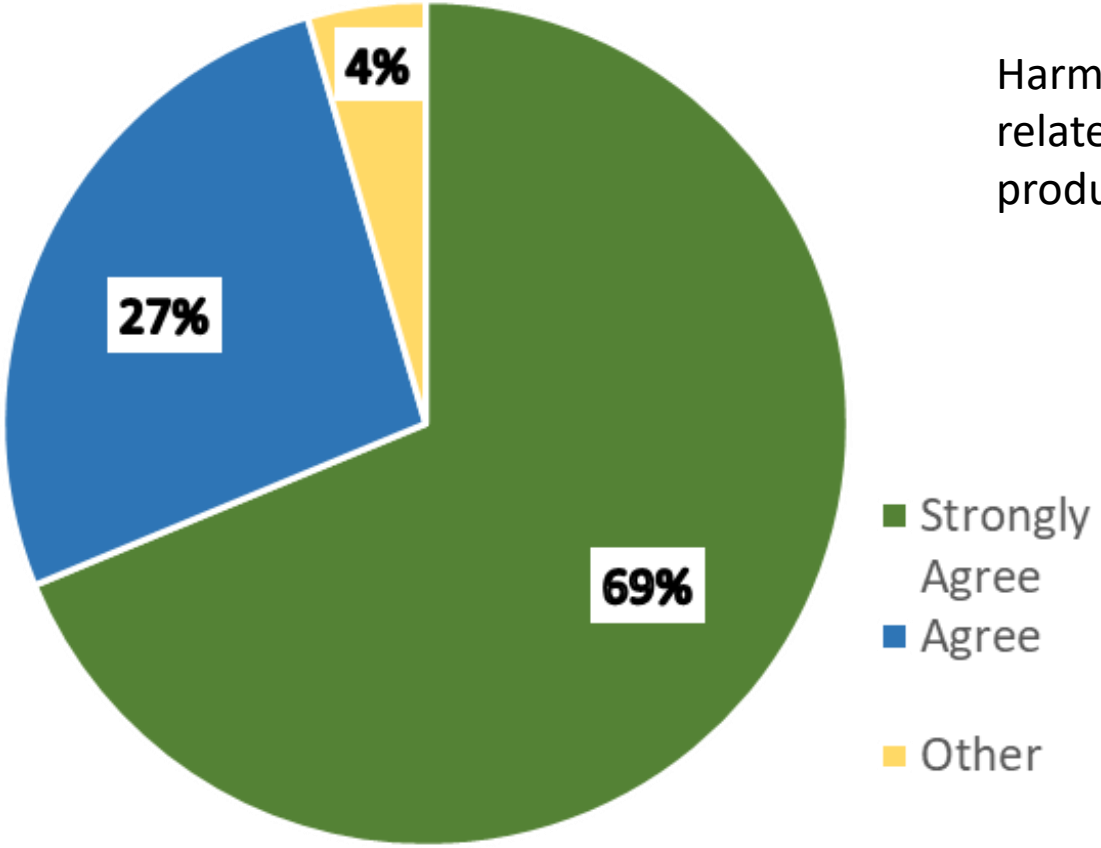


Breakout sessions:
How to lower hand in Webex?

- At the bottom center of Webex, select the **React** button,  , and tap **Lower hand**.



Agreement about the importance of a harmonized international approach



Harmonized international approach for regulatory standards related to the development and approval of complex generic products

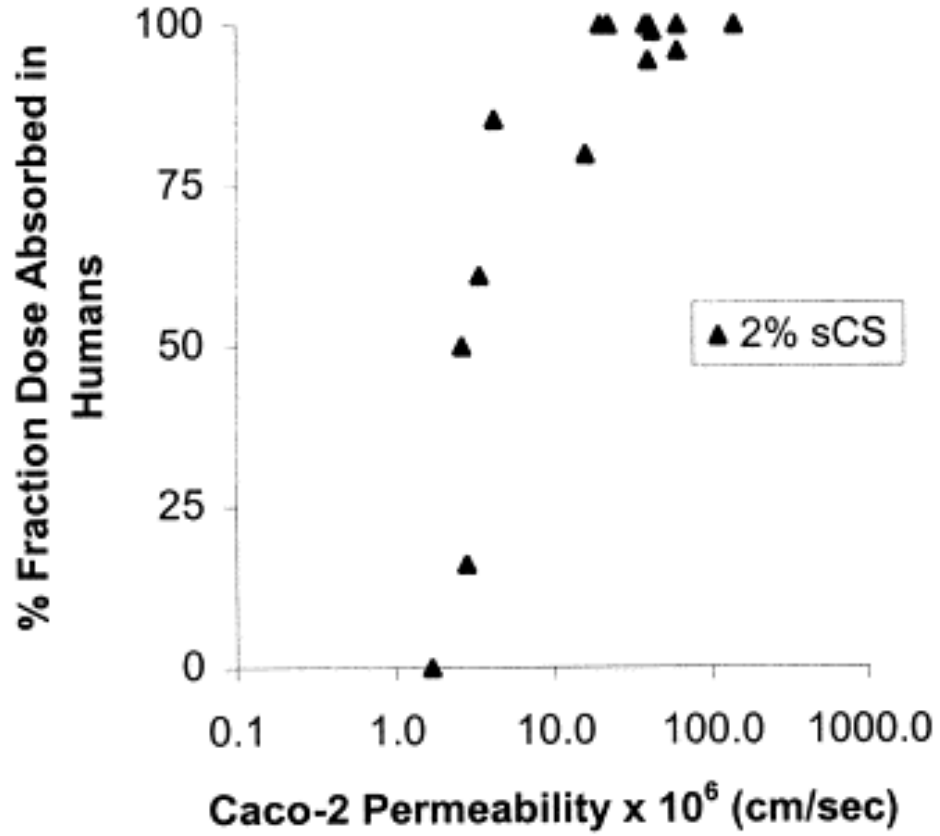
CENTER FOR RESEARCH ON COMPLEX GENERICS

www.complexgenerics.org

Brief BCS history

- Amidon, H. Lennernas, V.P. Shah, and J.R. Crison. A theoretical basis for a biopharmaceutic drug classification: the correlation of in vitro drug product dissolution and in vivo bioavailability, Pharm Res 12, 413–420, 1995
- Draft FDA BCS guidance published in 1999
- Final FDA BCS guidance published in 2000
- Wu and Benet BDDCS paper published in 2005
- WHO guidelines published in 2006
- EMA BE guidance published in 2010; FDA BCS guidance updated in 2017
- ICH M9 BCS guidance published in 2019

BCS regulatory applications are over 20 years old



Percent fraction dose absorbed in humans vs. Caco-2 permeability in the 2% supplemented calf serum (sCS) system.

Lentz, K.A., Hayashi, J., Lucisano, L.J. and Polli, J.E. (2000): Development of a more rapid, reduced serum culture system for Caco-2 monolayers and application to biopharmaceutics classification system. Int. J. Pharm. 200(1): 41-51

University of Maryland Center of Excellence in Regulatory Science and Innovation (M-CERSI)

- M-CERSI is an FDA-sponsored center at the Baltimore and College Park campuses of the University of Maryland (www.cersi.umd.edu).
- The mission of the Center is to foster the development of regulatory science – the science of developing new tools, standards and approaches to assess the safety, efficacy, quality and performance of FDA-regulated products.
- Thank you to Donna Blum-Kemelor, Tracey Lee, and Althea Cuff.

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Thank you

- Thank you for your attendance and participation!
- Thank you to all speakers, panelists, and breakout session moderators and scribes.
- Thank you to Dana, Ann, Melissa, Yuly, and Victoria.
- Special thanks to Mehul Mehta and Paul Seo.