Regulatory Education for Industry (REdI) and CERSI Workshop

Current State and Future Expectations of Translational Modeling Strategies to Support Drug Product Development, Manufacturing Changes and Controls

September 23-25, 2019

College Park, MD

DAY 1 - BREAKOUT SESSION B

Best Strategies for the development of biopredictive (clinically relevant) dissolution methods, a key element for successful modeling and simulation

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Session Background

- Dissolution testing can play a pivotal role throughout drug product development, however there are often challenges in linking *in vitro* testing to *in vivo* drug product performance.

- The advantage of setting up biopredictive dissolution conditions is that the *in vitro* dissolution profile can be used to predict the *in vivo* pharmacokinetic profile. Consequently, biopredictive dissolution method has application in formulation development, supporting formulation/manufacturing changes post-approval, setting up of clinically relevant dissolution specification.

- The purpose of this BO session is to define best strategies for the development of biopredictive dissolution methods, including a critical evaluation of the current gaps needing to be addressed, which is a key element for successful PBBM.

Session Background - Terminologies

Biorelevant dissolution method:

- A set of testing conditions for monitoring in vitro dissolution designed to closely mimic a relevant biological fluid and a physiological environment

Biopredictive dissolution method:

- A set of testing conditions for which in vitro dissolution profiles are capable of predicting pharmacokinetic profiles. These are typically based on classical or mechanistic IVIVC

Clinically relevant dissolution specifications:

- A set of in vitro dissolution conditions and acceptable criterion(ia), that can identify and reject drug product batches that are not expected to be bioequivalent to clinical pivotal product batches

Sandra Suarez-Sharp, et. al. Applications of Clinically Relevant Dissolution Testing: Workshop Summary Report. The AAPS Journal (2018), 20:93

Day 1 – BO Session B: Question 1

- **What are the approaches for development of a biopredictive dissolution method?**
  - **What data are needed for these approaches?**

Day 1 – BO Session B: Question 2

- **Should biorelevant factors be considered in media selection for biopredictive dissolution method development and when should they be applied (“one size fits all” or “horses for courses”)?**

Day 1 – BO Session B: Question 3

- **When developing a biopredictive dissolution method, should hydrodynamics factors, volumes and agitation be considered. How should these parameters be selected?**
  - **a. Are sink conditions always needed? In which circumstances?**
  - **b. What are the different approaches for achieving sink conditions and appropriate hydrodynamic conditions for the dissolution test?**
  - **c. What could be the decision strategy for the selection of dissolution apparatus (e.g. single vessel dissolution, two stage or multiple stage)?**

Day 1 – BO Session B: Question 4

- **In setting up a biopredictive dissolution method, how shall we go about validating not only the in vitro methods (e.g., dissolution and analytical) but also the in vivo predictability of the dissolution conditions?**

Overall Conclusions