Taro Pharmaceuticals

IVPT Data analysis -1

Topic: After plethora of investigations, some aberrant profiles were observed suggesting dose dumping which will inflate the CV% of the data (Figure 1). Importantly, such outcomes are not resulted from the poor study design or inadequate science and/or technology employed. The impact of such unexpected results may be quite disruptive to the study, conclusions and delays in the introduction of the generic products that indeed meet the IVPT requirements and are bio-equivalent.

Research Opportunity: Is the agency interested in an alternative statistical approaches or modelling to mitigate the impact of such data and if this research is conducted, could we have a guidance on the subject.

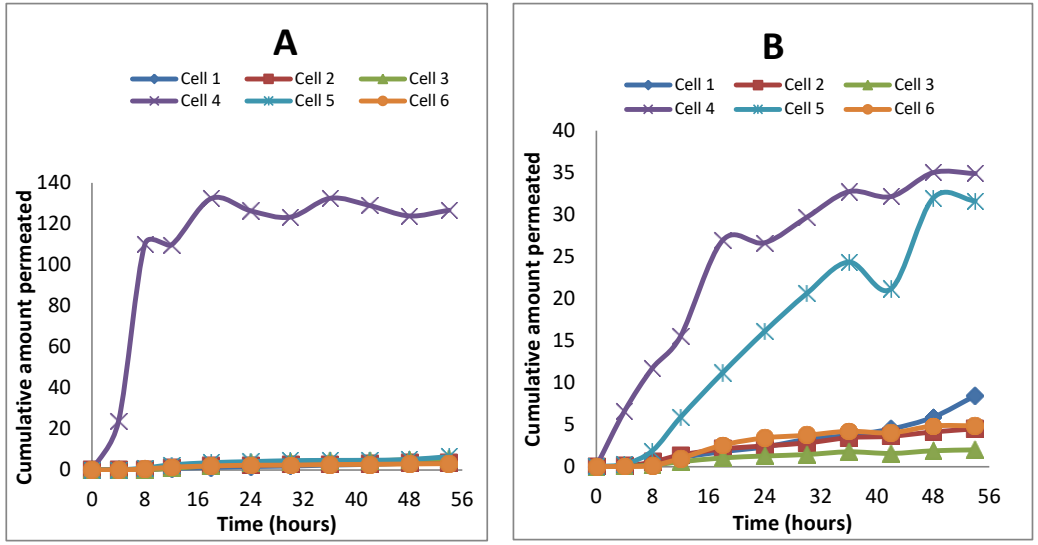

Figure 1 A: Proposed profile for dose dumping B: proposed profiles for a cell with no lag time and 30% of the data contributeto >50% RSD (Donor# 16)

IVPT Method development and Validation - 1

Topic: The FDA recommends the replacement of the entire receptor solution. However, with slow permeating molecules the existing strategies can create an analytical challenge.

Research Opportunity: Based on the FDA's research and academic and industry information, does FDA consider this factor as a major challenge and perhaps plans to further research other strategies or technologies such as partial receptor sampling?

Additional Note/Comment: The Acyclovir guidance propose the dose duration as representative method to demonstrate sensitivity. Have the agency published any details on this method? Is the agency planning to publish this data?

IVPT Method development and Validation - 2

Topic: There is a scientific evidence resulted from IVPT screening of different reference lots of some marketed products that show an evidence of performance differences within the RLD. A new thought is forming to compare multiple RLD and test lots. However, the design and statistics of such approach has not yet been investigated.

Research Opportunity: Have FDA considered such study designs and will you be willing to research such approach including development of appropriate statistics and acceptance criteria?

Additional Note/Comment: Due to COVID 19 pandemic, all elective surgeries are now seized. This shifts the supply chain to use cadaver skin. Have FDA researched various differences between the two type tissues? Are there any inclusion/exclusion criteria that the FDA investigated or recommended? Are there publications that can be shared?