“Research to Reality”- Can we bridge Regulatory Science Initiatives into policy for topical dermatological Drug Products?

Ravi S. Harapanhalli, Ph.D.
Senior Vice President
Global Regulatory Affairs
Amneal Pharmaceuticals

FDA Workshop on Topical Dermatological Generic Drug Products

October 20, 2017

amneal PHARMACEUTICALS

Current Situation

- Significant GDUFA resources being spent over years on regulatory science initiatives related to generic topical dermatological drug products
- Ongoing efforts to establish alternative, scientifically valid methods for evaluating TE of topical drug products
- How many generic topical dermatological drug products approved to date based on novel BE strategies?

Research to Reality?

- How far have we explored in vitro and in vivo cutaneous PK approaches to support an evaluation of BE?
- How does a panel of rationally selected in vitro and in vivo approaches to establish BE look like?
  - In vitro permeation test (IVPT)
  - In vitro release test (IVRT)
  - Dermal open flow microperfusion (dOFM)
  - Epidermal PK sampling by in vivo skin stripping
- QbD and enhanced knowledge on product and process
  - Linkage of CPPs to CQAs (physical, chemical, and microstructural)
- Do we need to link QbD info on generic drug to RLD?
  - No access to RLD QbD info

Relevance of Revised BE Guidance on Acyclovir Cream to other Topical Products?

- Four point criteria does not require dOFM or skin stripping
  - Q1/Q2 of test and RLD
  - Test and RLD products are physically and structurally similar based upon an acceptable comparative physicochemical characterization of a minimum of three lots of the test and three lots of the RLD product.
  - Equivalent rate of acyclovir release by vitro release test (IVRT) comparing a minimum of one lot each of the test and RLD products using an appropriately validated IVRT method.
  - Bioequivalence of test and RLD products based upon an acceptable in vitro permeation test (IVPT) comparing the rate and extent of acyclovir permeation through excised human skin from a minimum of one lot each of the test and RLD products using an appropriately validated IVPT method.

FDA's Approach to CCs for Topical Drug Products

- If no product-specific BE guidance recommending Q1/Q2 sameness to RLD
- FDA will not review proposed formulations that are not required/recommended to be Q1/Q2
- At best FDA provides Q1 related response but not Q2
- Can FDA consider providing Q2 related response as well to aid in product development so novel BE approaches can be applied?

amneal PHARMACEUTICALS