“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
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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?
Thank you!