A Science Based Approach to Overcoming Barriers to Development and Improving Patient Access to Dermatological Drug Products

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Generic Product Approval

- For product approval: PE + BE = TE
- Determination of BE is the biggest barrier towards approval of dermatological generic topical drug products
- An alternative approach needs to be developed that will assure drug product quality, safety and efficacy.
- A science based approach using SUPAC-SS principles and in vitro drug release measurement is developed (TCS) that can provide biowaiver for certain types of topical drug products.
- TCS will reduce regulatory burden without sacrificing in drug product quality and will improve patient access

Topical Drug Classification System, TCS

Q1, Q2 Same Q3 Same	TCS class 1
Q1, Q2 Same Q3 Different	TCS class 2
Q1, Q2 Different Q3 Same	TCS class 3
Q1, Q2 Different Q3 Different	TCS class 4

Ref: VP Shah et al., Int J of Pharmaceutics. 491: 21-25, 2015.

Topical Drug Classification System (TCS)

- **TCS** is a framework for classifying topical drug products based on its qualitative and quantitative composition, microstructure arrangements of matter and *in vitro* release (IVR).
- **TCS** is a classification system of topical drug products, which when applied will help in approval of generic topical drug products, without conducting *in vivo* studies, but assuring product efficacy.
- It is a drug development tool to justify 'biowaiver' in conjunction with the *in vitro* drug release of the topical dosage form.

Topical Drug Classification System (TCS)

- **TCS** is based on established scientific principles specifically developed for semisolid topical products (**SUPAC-SS**) and is combined with the **IVR** of the drug product.

- **TCS** considers the qualitative (**Q1**) and quantitative (**Q2**) composition, the role of inactive ingredients and microstructure arrangement of topical semisolid products (**Q3**).

- **Q3 → IVRT.**

Topical Drug Classification System - TCS

- Based on composition (**Q1** and **Q2**) and **IVR** properties, the topical drug products are classified as **TCS** class **1**, **2**, **3** and **4**.
- Under the proposed classification:
  - ❑Only **TCS class 1** and **TCS class 3** drug products are eligible for biowaiver;
  - ❑ **TCS class 2** and **TCS class 4**, are not eligible for biowaiver and will require *in vivo* BE studies for drug approval;
  - ❑The nature and type of *in vivo* BE study will depend on the therapeutic class and dosage form category.

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Topical Drug Classification System - TCS

Biowaiver

- **TCS Class 1:**
  Q1, Q2 and Q3 same → IVR
- **TCS Class 3:**
  Q1 and Q2 different, Q3 same → IVR

- **May require additional in vitro studies**
  (e.g., particle size, pH, globule size, rheology)
- Excipient evaluation

Bioequivalence Study

- **TCS Class 2:**
  Q1, Q2 same but Q3 different → BE studies
- **TCS Class 4:**
  Q1, Q2, Q3 different → BE studies

Acyclovir Cream

Current Study Findings

- 21 generic products and 6 RLD (from Europe, US) were analyzed.

Findings indicate that:

- The formulations (excipients/composition) are markedly different, the *in vitro* release and microstructure, rheology are all different.
- A good relationship was observed in these studies between microstructure (Q3) (rheology) and *in vitro* release.
- Changes in microstructure reflected in different release rate. **Q3 → IVRT**

Conclusion

- **A practical and science based classification system, TCS, for topical drug products is proposed.**

- TCS will facilitate:
  - ❑ Generic product development, reduce the regulatory burden and assure product quality across all therapeutic classes.
  - ❑ Availability of topical drug products to patients and consumers at a more reasonable cost.

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Thank you for your Attention