Analysis of ANDA Approval and Major Deficiencies

A Case Study with Topical Products

Advancing Generic Drug Development 2024:
Translating Science to Approval

Day 2, Session 6: Ensuring Efficient and Consistent High Quality Generic Drug Development

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Learning Objectives

- Discuss the ANDA landscape for topical products applied to the skin
- Identify challenges associated with the methodologies currently used to support product approval

Outline

- Recap of product-specific guidances (PSG) for topical products applied to the skin
- Landscape analysis of submitted ANDAs since Generic Drug User Fee Amendments (GDUFA) II – since FY 18
- Observed challenges and opportunities

Establishing Bioequivalence (BE) of Topical Products

Comparative clinical endpoint BE (CCEP BE) study

- In vivo BE study comparing the efficacy of a prospective generic product and the reference standard (RS), and both products are assessed to be superior compared to a placebo
- Can be used for: Majority of topical products

Vasoconstrictor (VC) study

- In vivo clinical BE study comparing the pharmacodynamic effect (i.e., skin blanching) of the prospective generic product and the RS
- Can be used for: Corticosteroid products

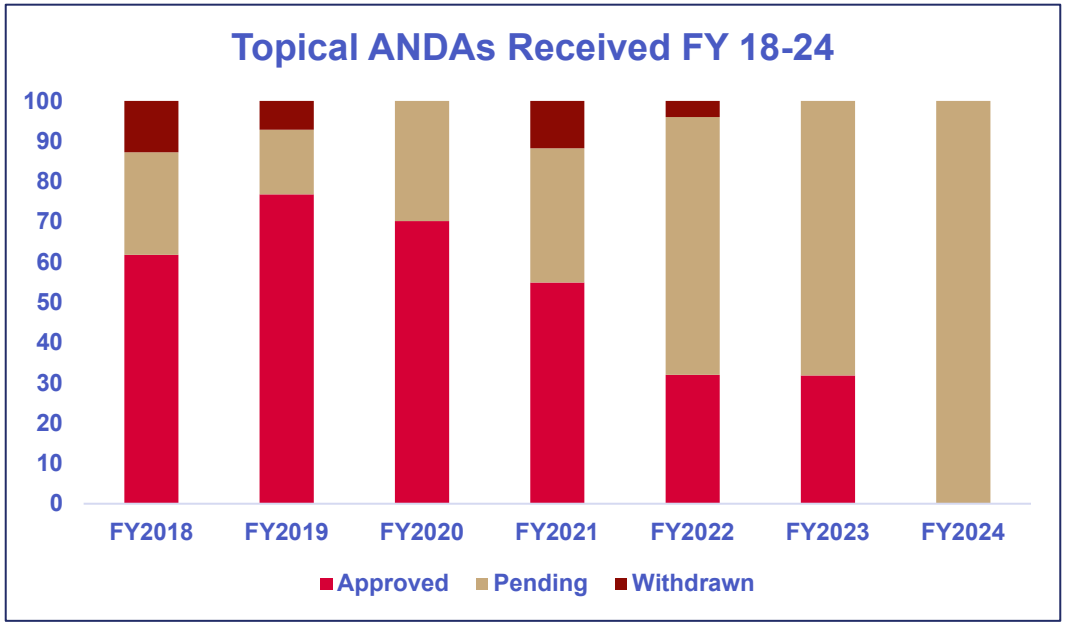
Waiver of in vivo BE studies

- Comparison of the formulation and/or dosage form of the prospective generic product and the RS
- Can be used for: Simple topical products (e.g., solutions)

Characterization-based BE approach

- Combination of in vitro and, in some cases, in vivo BE studies comparing formulation, microstructure, and performance of the prospective generic product and the RS
- Can be used for: Semisolid (e.g., gels, creams, etc.) topical products with certain formulations

Submitted Topical ANDAs



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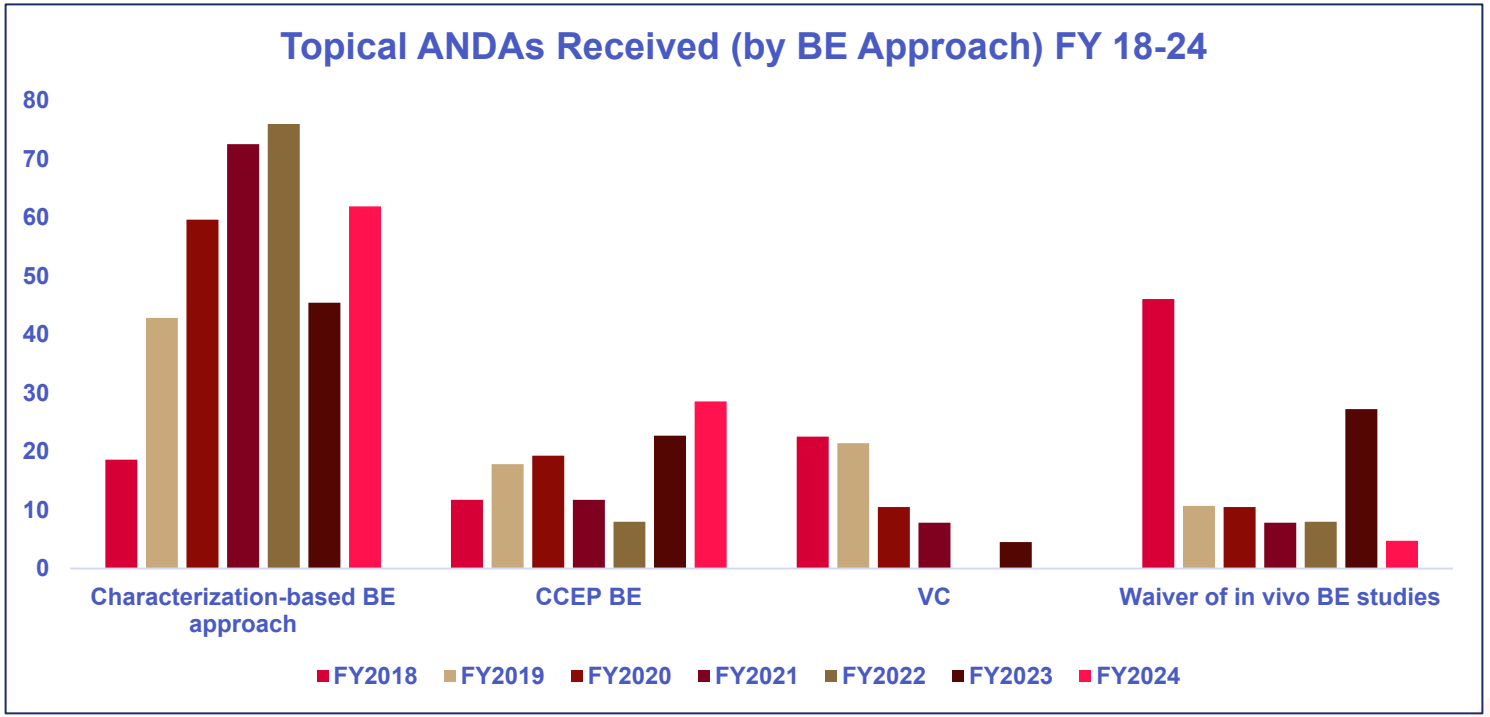
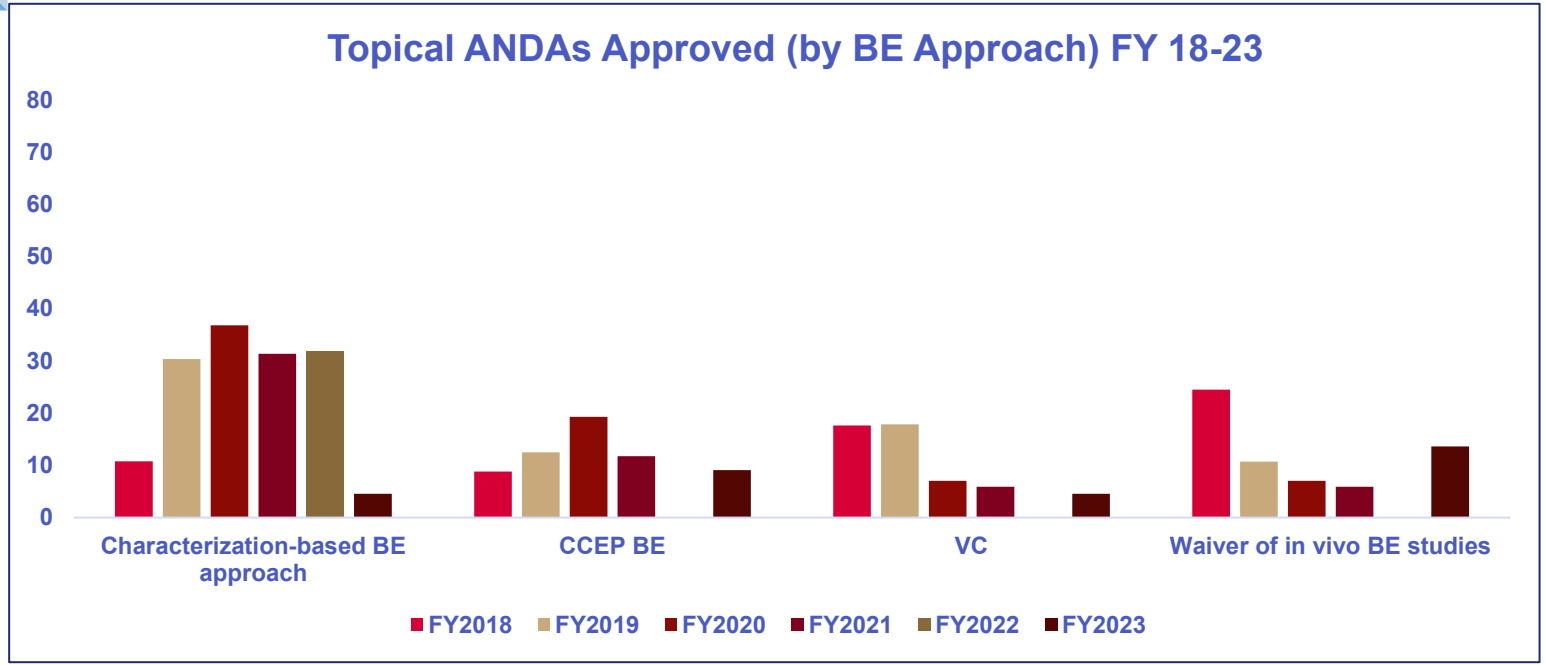


Data are normalized by total number of Topical ANDAs in a given FY
Application status as of June 30, 2024

Approved Topical ANDAs



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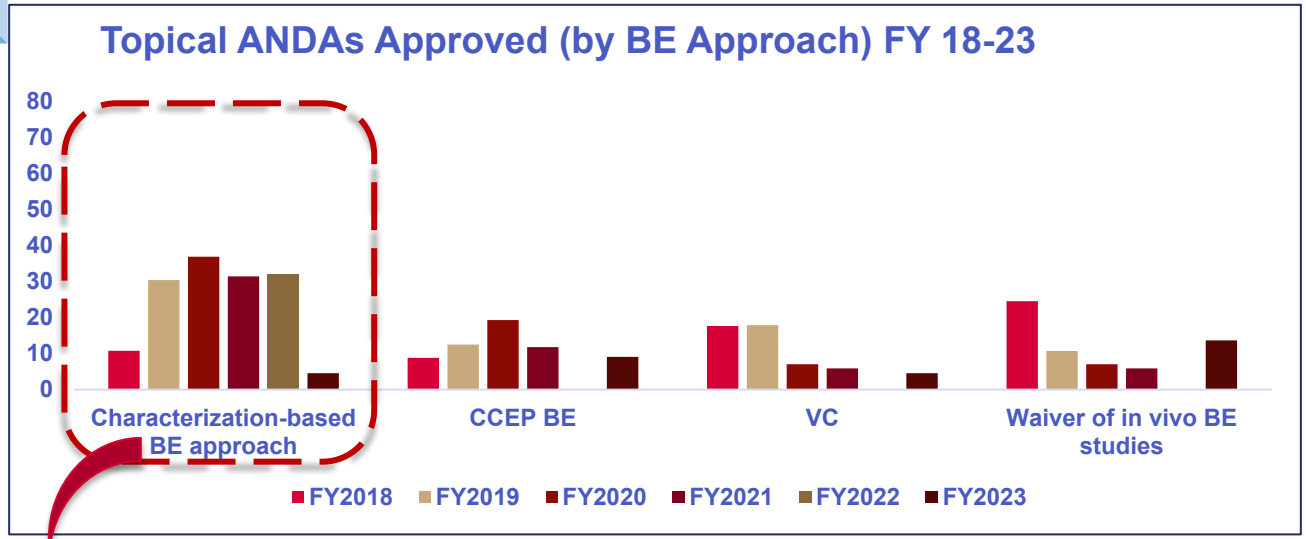
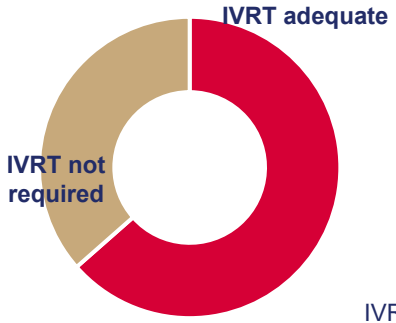
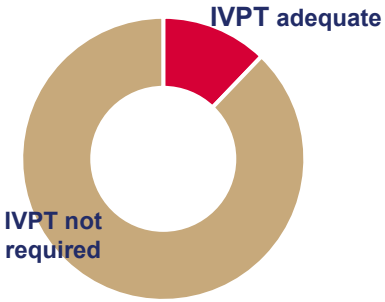
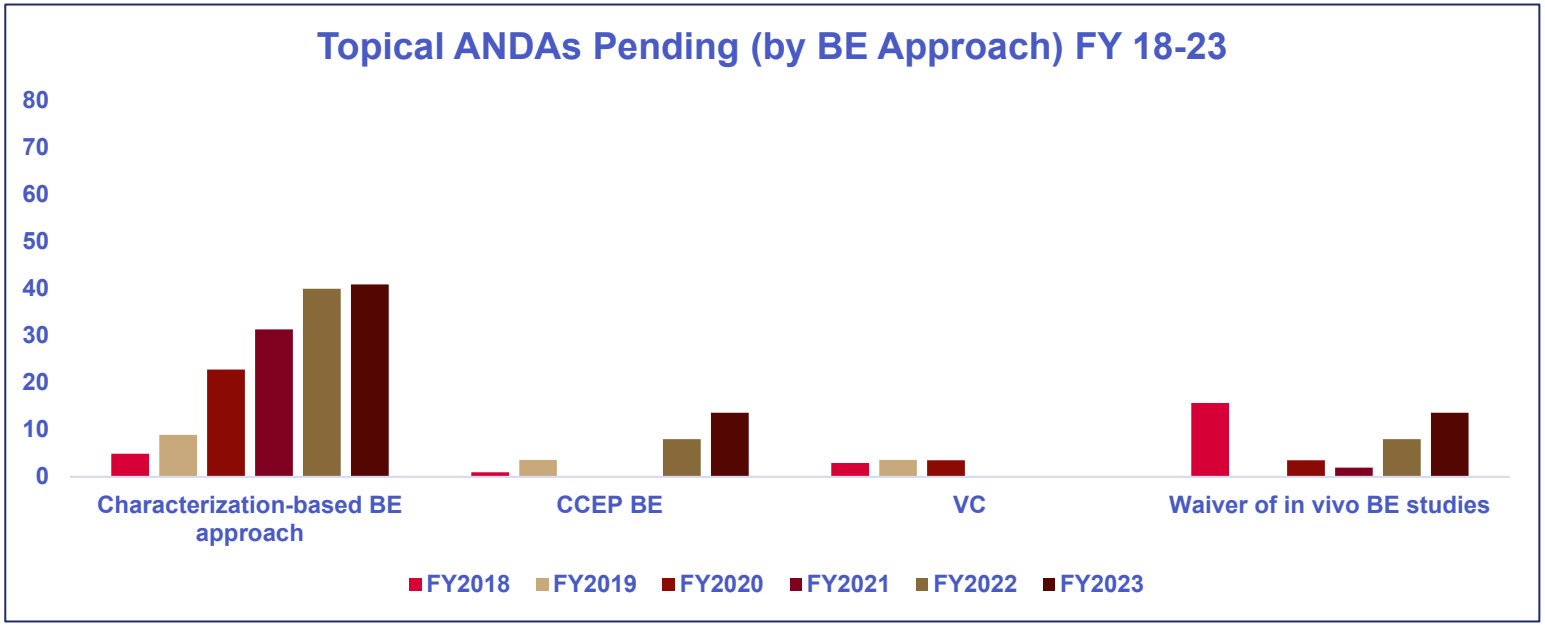






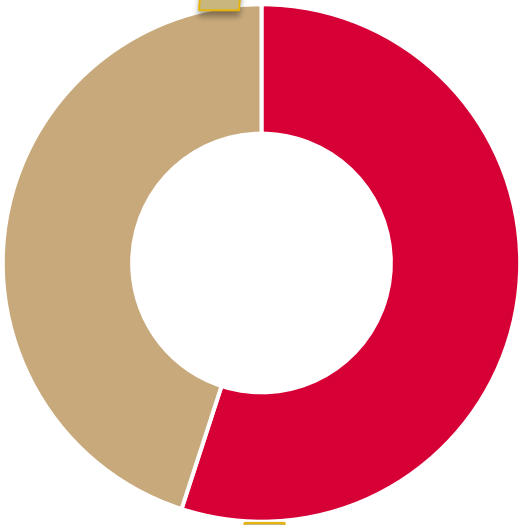
IVRT: In Vitro Release Testing
IVPT: In Vitro Permeation Testing

Pending Topical ANDAs



Data are normalized by total number of Topical ANDAs in a given FY
Pending ANDAs include ANDAs in pending and complete response status
Application status as of June 30, 2024

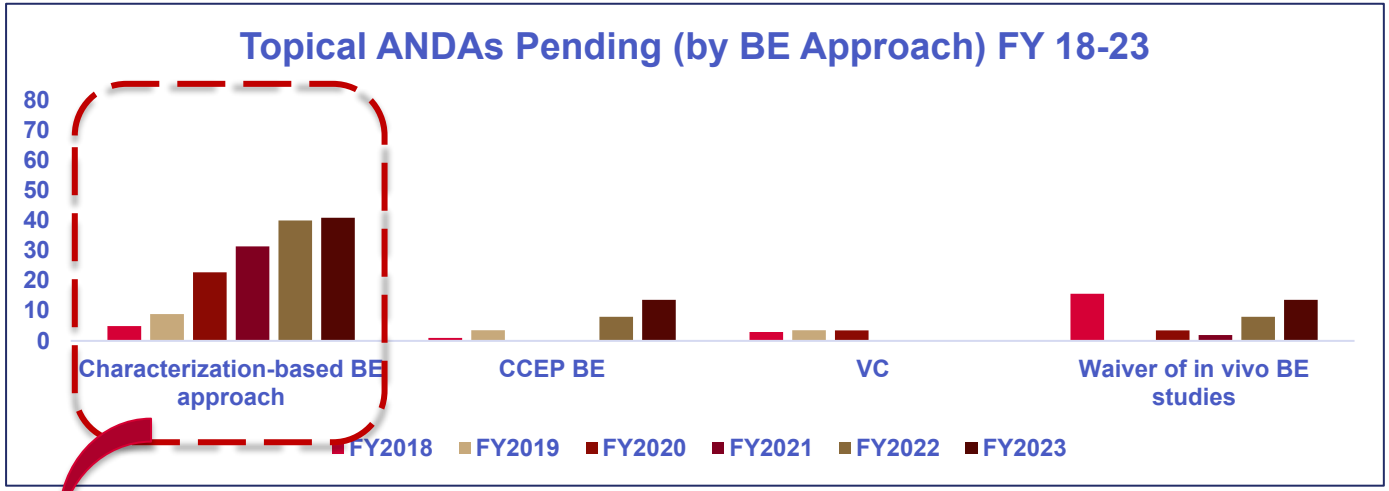
Challenges in Pending Topical ANDAs

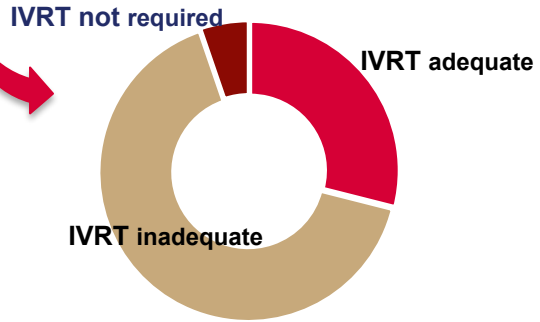


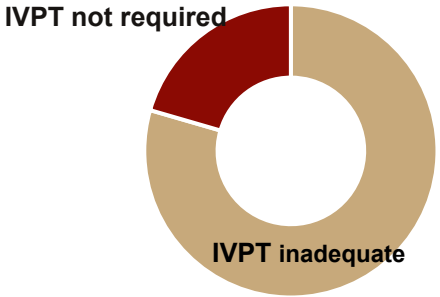
Outstanding challenges related to
- Bioequivalence
- Pharmaceutical quality
- Others (e.g., Labeling)

Outstanding challenges related to
- Pharmaceutical quality
  - Drug substance
  - Drug product
  - Manufacturing (& facility)
- Labeling

Challenges in Pending Topical ANDAs







Challenges in Topical ANDAs

IVPT

Challenges with Method Development

- Inadequate optimization of apparatus, receptor solution, dosing technique, sampling technique, sampling frequency

→ PDEV

Challenges with Method Validation

- Selection of dose/product for discrimination studies
- Assessing sensitivity and selectivity

→ PDEV or PSUB

Other Issues

- Aberrant Data

PDEV: Product Development Meeting
PSUB: Pre-Submission Meeting
https://www.fda.gov/drugs/news-events-human-drugs/redesigned-pre-submission-meetings-gdufa-iii-benefits-anda-submission-and-approval-05092024

Conclusions

- An analysis of the topical ANDA landscape suggests that characterization-based BE approaches have been predominantly used to support ANDA submission during GDUFA II, among other approaches
- >175 topical ANDAs received since FY 18, have been approved
- Among the pending ANDAs, challenges appear to be associated with the assessment of pharmaceutical quality, labeling and/or BE
- For ANDAs that utilized a characterization-based BE approach, there are significant challenges associated with IVPT studies, in particular
- Engagement with the Agency utilizing the PDEV and/or PSUB meetings can assist with resolving some of the observed challenges prior to submission of the ANDA

Challenge Question #1

What pathways can be used to interact with the Agency with challenges are identified related to IVPT study?

A. PDEV

B. PSUB

C. Post Complete Response Letter

D. Controlled Correspondence

E. All of the above

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Questions?

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