

AAPS/USP Webinar on USP Panel Findings on
Product Quality and Performance Tests for Topical and Transdermal Products
Development of a Novel In Vitro TDS Adhesion Test

August 13, 2024

Overview of the Topical and Transdermal Stimuli Article:

Advances in Product Quality and Performance Tests for Topical and Transdermal Products - View of the USP Expert Panel

Feedback to USP and Next Steps

Sam Raney, PhD

Associate Director for Science & Chief Scientific Advisor
Office of Research and Standards, Office of Generic Drugs
FDA Liaison to the United States Pharmacopeia (USP)

Overview of USP Stimuli Article

FDA

Purpose

- USP expert panel on *New Advancements in Product Performance Testing for Topical and Transdermal Products* authored a stimuli article
- Discussed current challenges and opportunities related to quality and performance testing in these areas
- Considered what compendial test methods and standards could support the development and assessment of future products
- Solicited public comments about how USP can contribute to the establishment of best practices and standards for such tests

Overview of USP Stimuli Article

Focus

- Identified three areas potentially needing new standards for technologies, equipment, test methods, and data analysis procedures:
 - In vitro adhesion tests for transdermal and topical delivery systems (collectively, TDS)
 - In vitro quality and performance tests for microneedle array systems
 - Physicochemical and structural (Q3) characterization tests for topical drug products
- Described the challenges related to developing novel product performance test methods for topical and transdermal drug products
- Sought to stimulate collaborative input and to harmonize research on the development of standardized test methods that could potentially be incorporated into future compendial chapters

Overview of USP Stimuli Article

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In Vitro TDS Adhesion Tests

- **Challenge:** Current compendial methods to evaluate the adhesive properties and adhesion performance of a TDS product are not designed to be biorelevant, and the results are difficult to interpret
- **Opportunity:** Novel tests could be developed to systematically evaluate the influence of numerous intrinsic and extrinsic factors on TDS adhesion performance (e.g., TDS properties and external stresses)
- **Impact:** Future in vitro adhesion tests results could provide more meaningful insights into the adhesion performance of TDS products when dosed on patients and worn under labeled use conditions

Overview of USP Stimuli Article

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Microneedle Array System Tests

- **Challenge:** Microneedle array systems (MAS) incorporate various design features that modulate the performance of these dosage forms via distinct mechanisms, implicating different critical quality attributes
- **Opportunity:** Novel mechanical tests for microneedle insertion and other tests for drug dissolution/release could be developed and standardized to characterize the influence of specific quality attributes
- **Impact:** Future tests could better emulate MAS product performance in vivo, guide the design of human factors studies, and facilitate the development of MAS products with optimal performance attributes for patients

Overview of USP Stimuli Article

Q3 Characterization Tests

- **Challenge:** Different test methods can sometimes be used to characterize a particular Q3 attribute in a product, and the different methods may not provide the same information, or be optimal to assess how that Q3 attribute modulates that product's performance
- **Opportunity:** Optimizing test methods and procedures for Q3 characterization of topical semisolid product attributes can establish a panel of standardized tests that are suitable for each context of use
- **Impact:** Future compendial methods and standards for Q3 characterization of topical semisolids can streamline the efficiency of topical product development and assessment

The Stimuli Article

In Vitro TDS Adhesion Tests

- The stimuli article proposed that novel tests should systematically consider how intrinsic TDS attributes and extrinsic environmental factors influence on TDS adhesion performance:
 - Examples of intrinsic attributes included TDS size, shape, adhesive type, adhesive system, adhesive formulation, TDS design, and the flexibility, stretchability, and occlusivity of the TDS backing membrane
 - Examples of extrinsic factors included the anatomically relevant temperature, curvature, torsion/flexion, softness, micro-topographical features, moisture, and flaking (micro-delamination) of the surface substrate used for the test

Feedback to USP

In Vitro TDS Adhesion Tests

- Public feedback to the stimuli article offered additional considerations:
 - Recommendations to consider the compatibility of specific adhesives with the surface substrate used to evaluate each and to consider substrates comprised of materials that have a similar surface energy to skin, unlike steel
 - Recommendations to consider additional extrinsic factors included elevated heat, cold, sweating, showering, swimming, and the impact of commonly used surfactants such as those found in body soaps and shampoos

CRCG Research Project

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In Vitro TDS Adhesion Tests

- The CRCG assembled academic, industrial and FDA experts who collaborated on the concept for a 5-year research project to:
 - Develop a theoretical framework for all the relevant intrinsic and extrinsic factors
 - Develop study designs and in vitro TDS adhesion tests using skin-mimetic substrates
 - Evaluate the in vitro adhesion performance of TDS products for which the FDA has access to comparative in vivo adhesion study results
 - Systematically modulate intrinsic TDS factors to alter adhesion performance across a range from excellent to poor, and use these to optimize the in vitro tests
 - Conduct adhesion studies with TDS products in vitro and in vivo under harmonized study conditions to evaluate whether in vitro results are predictive of in vivo performance in situations where the same intrinsic and extrinsic factors are present

CRCG Research Project

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In Vitro TDS Adhesion Tests

- The research project was awarded to Dr. Yousuf Mohamed at the University of Queensland, who will speak next to summarize research activities that have been initiated in his lab
- The moderated discussion that follows is intended to facilitate an interactive dialogue, and to solicit further input, about user requirements and scientific considerations that can guide this research
- Specifically, input is sought from investigators who work with TDS products to clarify what intrinsic properties and extrinsic factors are most likely to influence *in vivo* adhesion performance, and what features of the eventual test methods would be of practical value



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