Practical Considerations in the Selection of a Comparison Product for a Threshold Analysis

Jessica D. Sanford, Ph.D. and Krista I. A. Smith, M.Des

Overview

Threshold analysis is an established human factors assessment approach that compares a proposed drug–device combination product to an approved comparator across multiple medical product application types. Selection of an appropriate comparator product is critical to the success of a threshold analysis and is not always straightforward. This presentation provides practical considerations and lessons learned to support identification and selection of suitable comparator products for threshold analyses, which are increasingly used to justify that a medical device is safe and effective for its intended use.

While comparator selection may be simple when a clearly similar platform device is available, human factors teams often seek to conduct a threshold analysis without an obvious reference product or a defined strategy for narrowing potential options. This presentation offers practical guidance to support decision-making when selecting comparator products under these circumstances.

Threshold Analysis Process

Compare the differences between the reference product and the proposed comparison product to determine if there are no differences, minor differences, or other differences.

Comparative Task Analysis

Systematically dissect the use process for each product and examine and compare the sequential and simultaneous manual and intellectual activities for end-users interacting with both of the products in order to analyze the differences, with the goal to characterize the potential for use error.

Labeling Comparison (IFU, Carton, On-Body)

A side-by-side, line-by-line comparison of the full prescribing information, instructions for use, and descriptions of the delivery device constituent parts of the proposed product and the comparator reference product.

Device (and Constituent Parts) Comparison

Acquire the comparator reference product to examine (e.g., visual and tactile examination) the physical features of the comparator product and compare them to those of the delivery device constituent parts for the proposed combination product.

Relevant Guidance

- Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA. FDA Draft Guidance for Industry, January 2017
- Purpose and Content of Use Related Risk Analyses for Drugs, Biological Products, and Combination Products. FDA Draft Guidance for Industry and FDA Staff, July 2024
- Bridging for Drug-Device and Biologic-Device Combination Products. FDA Draft Guidance for Industry, December 2019
- Contents of a Complete Submission for Threshold Analyses and Human Factors Submissions to Drug and Biologic Applications. FDA Draft Guidance for Industry and FDA Staff, September 2018
- Content of Human Factors Information in Medical Device Marketing Submissions. FDA Draft Guidance for Industry and FDA Staff, December 2022

Choosing the Right Product

Considerations in the Selection of a Comparison Product

Labeling

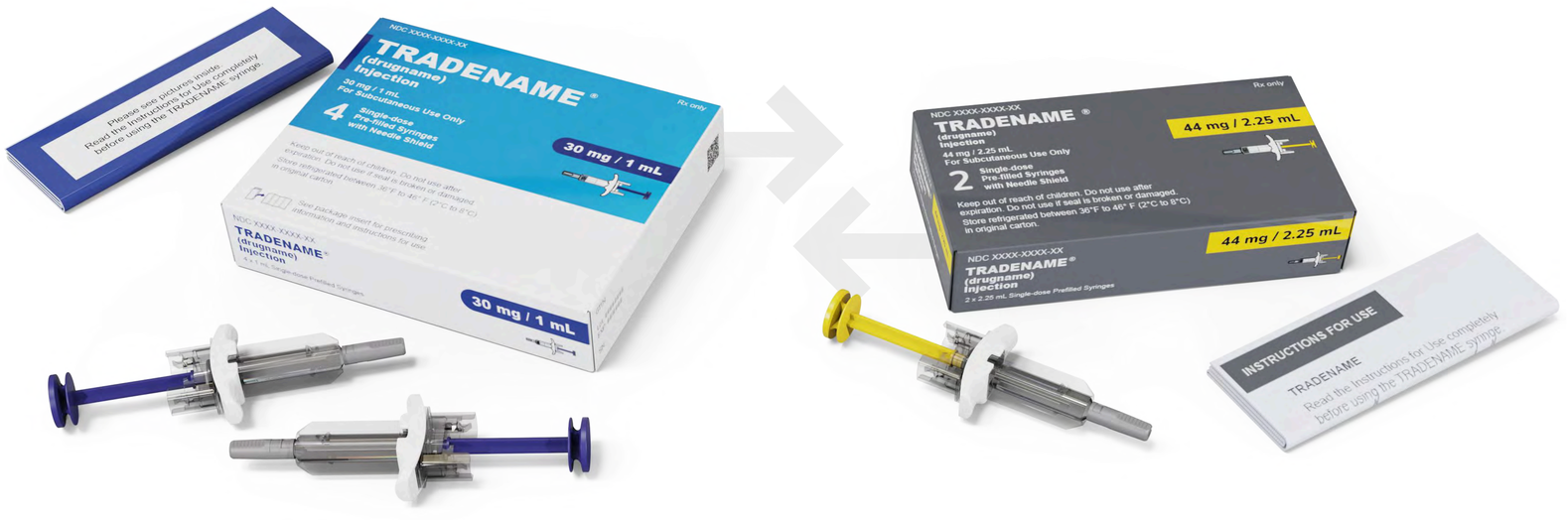
- Determine if comparator has successful labeling/IFU content and structure or if there is a need for change
- Evaluate if the labeling/packaging is reproducible and/or if there are manufacturing or patent limitations
- See if manufacturing differences impact risks (IFU fold patterns, carton closure, label legibility, etc.)
- All on body labels on a device need evaluated for content and structure

Device Components

- Evaluate whether the device is a platform product with similar devices on the market or a standalone product
- Compare customization of components (color, size, viewing window, dose levels, activation force and torque, etc.) and the most desirable comparison product
- Consider impact of any implemented or intended device improvements
- Don't forget to evaluate tactile and audible feedback

Task Analysis

- See if all tasks and order align, if there are any additional or omitted tasks, or any meaningful variation in order of tasks
- Evaluate impact of differences on critical tasks identified in a Comparative URRA (Use Related Risk Analyses)
- Assess if the intended use and treatment regimen (frequency, amount/number of doses, storage, etc.) create task differences with associated differences in packaging and user interaction



Users

- User specifications show if population characteristics can impact product use
- Consider user characteristics (age, medical condition and progression, cognitive and physical impairments, etc.) that may impact interactions with the device and/or labeling
- Determine if there are differences in the device that greatly impact the way the user interacts with it to use or administer the drug product
- Take into account all potential user cohorts and differing interactions each group has with the device

Other Considerations

- Timing of comparison product selection can impact design: if early in the development process then can design to minimize differences, if later then can only select and evaluate impact of any differences
- Consider ability to acquire the comparison product and/or product data
- Comparisons to a product no longer on the market is possible, but offers challenges
- The URRAs for the products play a key role in all comparisons and the determination of critical tasks as part of the larger comparative study
- Engage with FDA in selection of the comparison product to receive helpful feedback and foster submission success
- Comparison products are often those on the market, but other products in the pipeline can be leveraged as a comparison product
- After completion of threshold analysis, determine if supplemental data (differentiation study, engineering testing, label comprehension, etc.) is needed to support threshold analysis results and/or if user interface modifications to the device or labeling are needed to minimize differences