Pre-ANDA Program Support of Generic Drug-Device Combination Products

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Presentation Objectives

- Discuss how and when the user interface of a proposed generic drug-device combination product is evaluated.
- Explain how to seek advice regarding user interface assessment of generic drug-device combination products.
- Review device and user interface recommendations in product-specific guidance.

Substitutability of Generic Drug-Device Combination Products

- In addition to the approval requirements for all Abbreviated New Drug Applications (ANDAs), several additional factors are considered in ANDA review process regarding substitutability of drug-device combination products:
  - Performance characteristics
    - FDA takes into consideration the performance of the device constituent and its interaction and impact on the delivery of the drug constituent
  - User interface considerations - the focus of this presentation

Generic Drug-Device Combination Product Substitutability

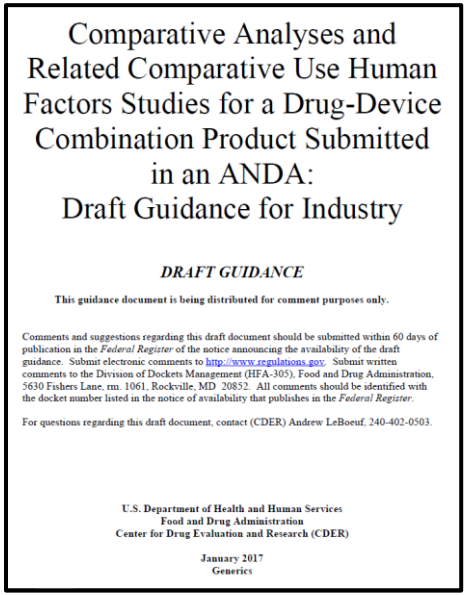
- Potential applicants should carefully consider design of user interface of proposed drug-device combination products and minimize differences from the reference listed drug (RLD).
- What is meant by “User Interface?”
  - Includes all components of the product with which a user interacts:
    - Delivery device constituent of combination product
    - Any associated controls and displays
    - Product labeling and packaging

Assessing the User Interface: Comparative Analyses

- Proposed generic and RLD user interfaces are evaluated through comparative analyses.
- Three analyses for comparing device user interface of the proposed generic combination product to the user interface of the RLD.
  - Physical comparison
  - Task analysis
  - Labeling comparison
    - Pre-ANDA program focuses on Instructions For Use (IFU) labeling comparison
- Comparative analyses methodology will be discussed in more depth in the next presentation.

Draft Guidance for Industry Regarding Comparative Analyses

- Comparative analyses should be conducted during product development phase to understand differences of proposed generic user interface as compared to RLD.
- Potential applicants are encouraged to submit comparative analyses to FDA for review in Pre-ANDA Program.
- Should be included in original ANDA submission.
- 2017 Draft Guidance for Industry on Comparative Analyses.
  - Access at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/comparative-analyses-and-related-comparative-use-human-factors-studies-drug-device-combination



Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA:
Draft Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Andrew LeBoeuf, 240-402-0503.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

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Generics

Pre-ANDA Program Support for Applicants Developing Drug-Device Combination Products

- Avenue for communication about user interface of proposed generic drug-device combination products:
  - Controlled Correspondence
  - Pre-ANDA Product Development meeting
    - Designed to facilitate approval of complex generic drug products, including complex drug-device combination products.
- Publishing product-specific guidances (PSGs) with device and user interface considerations.

Controlled Correspondences: Requests Related to Evaluation of User Interface*

- Addresses specific questions related to evaluation of user interface of drug-device combination product.
- Submissions should include:
  - Comparative analyses
  - Specific question about user interface (questions related to quality should be submitted in a separate controlled correspondence)
  - Three samples of proposed generic and RLD.
    - If multiple strengths are proposed, include three samples of each strength (proposed generic and RLD) unless the device user interfaces of the different strengths are identical except for color scheme and labeling information. In this case, three samples of one strength (proposed generic and RLD) and one sample of each of the other strengths are sufficient.
    - If samples are prototypes, the correspondence should specify as such and identify any components (including device labeling) that have been omitted or are still in development

*Draft guidance for Industry. *Controlled Correspondence Related to Generic Drug Development* (Dec 2022). https://www.fda.gov/media/164111/download

Pre-ANDA Product Development Meeting: Requests Related to Evaluation of User Interface*

- Generally discusses scientific issues or questions that involve multiple disciplines and multiple questions related to product development.
  - Generally for complex products, including complex drug-device combination products (e.g., pre-filled auto-injectors, metered dose inhalers)
- Same information regarding drug-device combination product should be provided as discussed on previous slide.

*Guidance for Industry. *Formal Meetings between FDA and ANDA Applicants of Complex Products Under GDUFA* (Oct 2022). https://www.fda.gov/media/107626/download

Pre-ANDA Program Support for Applicants Developing Drug-Device Combination Products

- FDA recommends applicants use and follow draft guidance for industry *Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA* for assessing user interface of proposed generic.

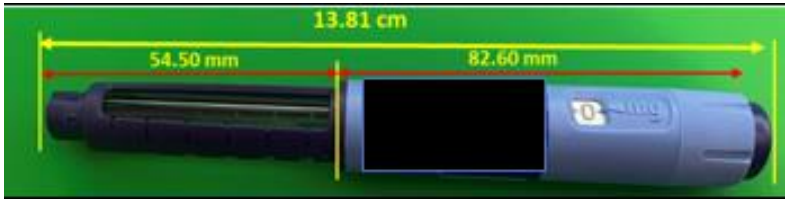
- Device samples should be mailed to:

  Office of Research and Standards/Office of Generic Drugs
  U.S. Food and Drug Administration
  10903 New Hampshire Avenue
  Building 75, Room 4723
  Silver Spring, MD 20993

- Comparative Use Human Factors (CUHF) study protocols may be submitted in either Pre-ANDA Product Development Meetings or Controlled Correspondences for review.

FDA Review of and Response to Comparative Analyses in Pre-ANDA Program

- FDA reviewers review firm's comparative analyses.
- FDA may provide advice on whether there are "minor" or "other" design differences between the proposed generic and RLD.
- Level of detail for physical comparison includes dimensions, shape, color, texture, functionality of device components.



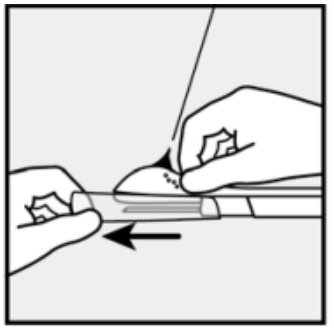
*Depictions are hypothetical and for illustrative purposes only

Product Specific Guidance (PSG): Device Recommendations

- PSGs are published by FDA.
- Describes Agency's current thinking and expectations on how to develop generic drug products that are therapeutically equivalent to the RLD.
  - https://www.accessdata.fda.gov/scripts/cder/psg/index.cfm
- Objectives for incorporation of device language:
  - Provide transparent information/recommendations to industry
  - Provide consistent recommendations for similar device types/device user interfaces

Example of PSG with Device and User Interface Recommendations

- Etonogestrel Implant
- NDA 021529
- Indicated for use by women to prevent pregnancy.
- Long-acting (3-years), reversible, hormonal contraceptive.
- Implant is preloaded in a disposable applicator.
- Administered/removed by healthcare professional in clinic.

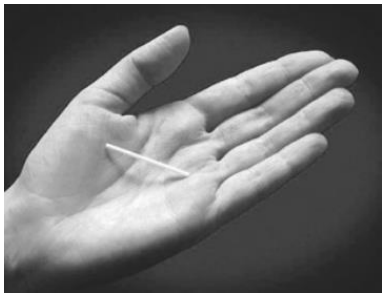


Etonogestrel Implant, NDA 021529, PSG (Cont.)

Additional information:

Device Subheading

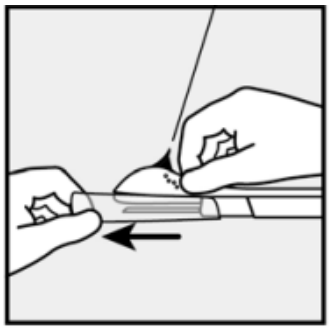
Device:
The reference listed drug (RLD) product is presented as a removable implant in a disposable applicator. The implant and the applicator are device constituents used to administer the drug.



Recommendations to consider

FDA recommends that prospective applicants examine the size and shape, external critical design attributes, and external operating principles of the RLD devices when designing the test devices including the following characteristics:

- Radiopaque implant
- Preloaded, single-use applicator
- Gauge and length of applicator needle



User Interface Assessment Subheading

User Interface Assessment:
An ANDA for this product should include complete comparative analyses so FDA can determine whether any differences in design for the user interface of the proposed generic product, as compared to the RLD, are acceptable and whether the product can be expected to have the same clinical effect and safety profile as the RLD when administered to patients under the conditions specified in the labeling. For additional information, refer to the most recent version of the FDA guidance for industry on *Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA.*[a]

Device Subheading

- Statement of how the RLD is presented or what the RLD is.

> Device:
> The reference listed drug (RLD) product is presented as a removable implant in a disposable applicator. The implant and the applicator are device constituents used to administer the drug.

- This statement is specific to the RLD device constituent, and statement will change based on the RLD.
- Additional examples:
  - The RLD is presented in a nasal pump dispenser that is a device constituent.
  - The RLD is presented as single-dose, prefilled syringe cartridges that are co-packaged with an autoinjector pen and a carrying case. The autoinjector pen is the device constituent.

Device Characteristic Recommendations

- Statement about device aspects of RLD FDA recommends the firm consider when designing the test device.

> FDA recommends that prospective applicants examine the size and shape, external critical design attributes, and external operating principles of the RLD devices when designing the test devices including the following characteristics:
>
> - Radiopaque implant
> - Preloaded, single-use applicator
> - Gauge and length of applicator needle

- "FDA recommends…" is consistent language included in all device recommendations.
- Bullet point considerations take into account end-user and use-environment of the RLD product and change based on RLD.

User Interface Assessment Statement

- Provides recommendations for conducting comparative analyses and references the guidance.

User Interface Assessment:
An ANDA for this product should include complete comparative analyses so FDA can determine whether any differences in design for the user interface of the proposed generic product, as compared to the RLD, are acceptable and whether the product can be expected to have the same clinical effect and safety profile as the RLD when administered to patients under the conditions specified in the labeling. For additional information, refer to the most recent version of the FDA guidance for industry on *Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA.*[a]

Conclusions and Recommendations

- Engage with FDA during product development through Pre-ANDA Program to request feedback on the proposed generic drug-device combination product user interface.
- Comparative analyses are an iterative part of generic drug-device combination development.
- Access product-specific guidances to identify recommendations for device constituents during product development.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