Generic Drug–Device Combination Products: Evaluating Combination Products & Navigating Differences

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Learning Objectives

- Discuss statutory and regulatory sameness considerations for generic drug-device combination products

- Review the comparative analyses (CA) process used to evaluate the sameness of generic drug-device products as compared to the reference listed drug (RLD)

Statutory and Regulatory Considerations

- **Section 505(j) of the Federal Food, Drug, and Cosmetic Act**
  - An abbreviated new drug application (ANDA) generally must contain information to show that the proposed generic product (1) is the same as the RLD with respect to the active ingredient(s), conditions of use, route of administration, dosage form, strength, and labeling (with certain permissible differences) and (2) is bioequivalent to the RLD

- **Therapeutic equivalents**
  - Approved drug products that are pharmaceutical equivalents for which bioequivalence has been demonstrated, and that can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling (21 CFR 314.3(b))

Generic Drug–Device Combination Products

- **Therapeutic equivalents**
  - "**.** . . can be expected to have the *same clinical effect and safety profile* when administered to patients under the *conditions specified in the labeling.*"

- **Same expectations** apply for generic drug-device combination products
  - FDA considers whether end-users can use the generic combination product when it is substituted for the RLD
    - Without the intervention of a healthcare professional *or*
    - Without additional training prior to the use of the generic combination product

- Generic and RLD products do not need to be identical
  - As long as the differences do not preclude approval under an ANDA

Comparative Analyses

Comparative Analyses Process

Key Players

OGD Division of Therapeutic Performance I (DTP I)

- Lead for pre-ANDA CA assessments

OGD Division of Clinical Review (DCR)

- Lead for ANDA and post-approval CA assessments

OSE Division of Medication Error Prevention and Analysis I and II (DMEPA)

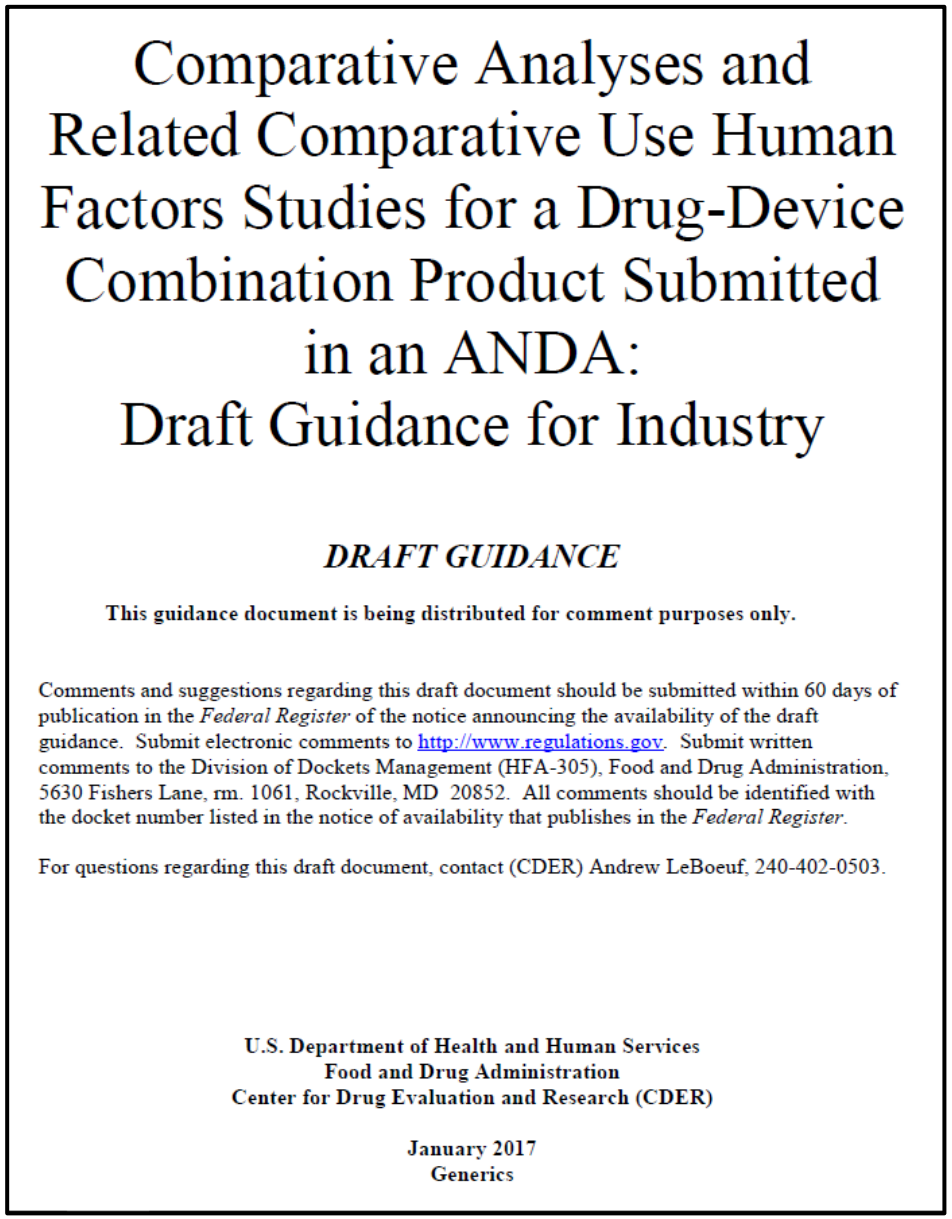
- Lead for CUHF* study and protocol assessments

Office of Biostatistics, Division of Biometrics VIII

- Statistical lead for CUHF study assessments

*CUHF-Comparative Use Human Factors

Draft Comparative Analyses Guidance



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.

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Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

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Generics

Labeling comparison: FDA recommends 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 generic combination product and its RLD.

Comparative task analysis: FDA recommends that potential applicants conduct a comparative task analysis between the RLD and the proposed generic combination product.

Physical comparison *between RLD and generic device constituent parts:* FDA recommends that the potential applicant of the proposed generic combination product acquire the RLD to examine and compare (e.g., visual and tactile examination) the physical features of the user interfaces of the RLD and proposed generic products.

Access at:
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/comparative-analyses-and-related-comparative-use-human-factors-studies-drug-device-combination

Key Definitions

User Interface (UI)

- All components of the product with which a user interacts
- Includes delivery device constituent part and any associated controls, displays, product labeling, and packaging

Critical Task

- A user task that, if performed incorrectly or not performed at all, would or could cause harm to the patient or user, where harm is defined to include compromised care

External critical design attribute

- A feature that directly affects how users perform a critical task that is necessary in order to use or administer the drug product

Comparative Analyses Outcomes

- For each physical, task, or labeling comparison performed during CA, provide one of the following outcomes:
  - **No Differences**
  - **Minor Design Difference**
    - If the difference in the user interface of the proposed generic combination product, in comparison to the user interface of the RLD do not affect an external critical design attribute
  - **Other Design Difference**
    - If any aspect of the comparative analyses suggests that difference in the design of the user interface of a proposed combination product as compared to the RLD *may* impact an external critical design attribute that involves administration of the product
- Consider any identified differences in the context of the overall risk profile of the product

Comparative Analyses: Best Practices

- Identify ALL user interface differences
- Classify ALL differences based on definitions in the guidance
- Focus on potential differences in the critical tasks between the RLD and proposed generic drug-device combination products.
  - Remember that **not every task is a critical task**
- Consider the product and its context of use
  - Same difference could be classified and assessed differently
  - Focus on individual RLD

Best practice: Always consider context of use

Context of use

- **Urgency of use**: Emergency vs. non-emergency
- **Frequency of use**: Single use vs. repeated use
- **End-users**: Patients, caregivers, healthcare professionals
- **Environment of use**:
  - Clinical: hospital, clinic
  - Nonclinical: home, school, etc.
- **Patient population**:
  - Dexterity issues (rheumatologic, neuromuscular disorder)
  - Incapacitated (naloxone HCl)