
POLICY AND PROCEDURES

OFFICE OF GENERIC DRUGS
**Assessment of the User Interface of a Drug-Device Combination Product Submitted
in a Pre-ANDA Communication or an ANDA**

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PURPOSE

The purpose of this MAPP is to describe how the Office of Generic Drugs (OGD) and the Office of Surveillance and Epidemiology (OSE) will assess the user interface of a drug-device combination product (generic combination product). The policies and procedures outlined in this MAPP apply to all generic combination products.

BACKGROUND

FDA's draft guidance for industry, *Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA*, provides a systematic approach for abbreviated new drug application (ANDA) applicants to use in identifying and analyzing differences between the user interface of a proposed generic combination product and the user interface of its reference listed drug (RLD).¹ As described in that guidance, applicants should first perform comparative analyses to identify all differences between the user interface of the generic combination product and the user interface of the RLD. If differences are identified, applicants should classify

¹ When final, this guidance will represent the current thinking of FDA. For the most recent version of a guidance, visit FDA's guidance webpage: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>. *Reference listed drug* is the listed drug identified by FDA as the drug product upon which an applicant relies in seeking approval of its ANDA.

each identified difference as a “minor design difference” or “other design difference.” In certain instances, the presence of an other design difference between the proposed generic combination product’s and RLD’s user interfaces may warrant submission of additional information and/or data beyond the comparative analyses, such as data from comparative use human factors (CUHF) studies, to further assess the acceptability of the identified difference(s).

Both OGD and OSE have differing expertise that may inform the review of comparative analyses of generic combination products. This MAPP clarifies OGD’s and OSE’s roles and responsibilities for the assessment of comparative analyses and CUHF studies, explains when OGD will consult OSE, and outlines OGD’s and OSE’s policy for regularly scheduled meetings between OGD and OSE to support shared learning, awareness, and consistency, where applicable, in the assessment and characterization of user interface differences for combination products submitted under different application pathways (e.g., 505(j), 505(b)(2), and 351(k)).²

POLICY

- OGD’s Division of Therapeutic Performance I (DTP I) in the Office of Research and Standards reviews comparative analyses and questions about the user interface that are submitted in pre-submission controlled correspondence³ and pre-ANDA meeting requests.
- OGD’s Division of Clinical Review (DCR) in the Office of Safety and Clinical Evaluation reviews comparative analyses and questions about the user interface submitted in ANDAs and in other correspondence sent to the Agency after ANDA submission.
- OSE’s Divisions of Medication Error Prevention and Analysis I and II (DMEPA) review comparative analyses when consulted by DTP I or DCR. DTP I and DCR may consult DMEPA to review comparative analyses as appropriate to assist in answering questions, including regarding the acceptability of any design differences identified between a generic combination product and its RLD.⁴

² OGD has responsibility for evaluating the user interface of a generic combination product submitted in an ANDA under section 505(j) of the Federal Food, Drug and Cosmetic Act. DMEPA has responsibility for the comparative evaluations of drug-device and biologic-device combination products submitted in 505(b) new drug applications and 351(a) and 351(k) biologics license applications and the review of protocols for and results from comparative use human factors studies.

³ For the purposes of this MAPP, *pre-submission controlled correspondence* refers to controlled correspondence sent to the Agency before an ANDA has been submitted.

⁴ OGD may, for example, consult DMEPA to respond to inquiries in cases where OGD determines that DMEPA’s medication and use error prevention or human factors expertise may be appropriate to answer questions.

- DTP I consults DMEPA to review CUHF study protocols submitted in pre-submission controlled correspondence and pre-ANDA meeting requests.
- DTP I generally does not consult DMEPA if CUHF study results are submitted in a pre-submission controlled correspondence or pre-ANDA meeting request; instead, DTP I advises the applicant that those results cannot be reviewed in such pre-ANDA communications and they should instead be submitted as part of the original ANDA submission.⁵
- DCR consults DMEPA to review CUHF study protocols and CUHF study results that are sent to the Agency after an ANDA has been submitted, including in response to a complete response letter.
- DTP I, DCR, and DMEPA will engage in regular, recurring meetings to support shared learning, awareness, and consistency in the assessment and characterization of user interface differences for combination products submitted under different application pathways. Examples of topics that may be presented for discussion include:
 - Novel and/or challenging comparative analyses
 - Products that pose novel policy considerations that may potentially impact multiple regulatory programs and application pathways (e.g., 505(j), 505(b), 351(a), and 351(k))
 - Data submitted by the applicant from something other than a CUHF study to support the acceptability of an other design difference
 - Unusual review situations (e.g., an ANDA applicant submits a CUHF study protocol or study results before OGD has reviewed the comparative analyses and confirmed there are other design differences).

RESPONSIBILITIES

- **OGD's Division of Therapeutic Performance I (DTP I)**: DTP I responds to inquiries on comparative analyses that are submitted in pre-submission controlled correspondence and pre-ANDA meetings and determines whether there are minor

⁵ If a prospective applicant submits a pre-submission controlled correspondence or pre-ANDA meeting request seeking FDA's feedback on how to address CUHF study results, and the prospective applicant has concluded those results fail to demonstrate that an other design difference is acceptable, DTP I may consult DMEPA for feedback on additional CUHF studies or alternative approaches to address the other design difference.

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- design differences and/or other design differences. DTP I consults DMEPA on comparative analyses as needed and on all CUHF study protocols. DTP I also participates in regularly scheduled meetings with DCR and DMEPA to support shared learning, awareness, and consistency in the assessment and characterization of user interface differences for combination products submitted under different application pathways.
- **OGD's Division of Clinical Review (DCR):** DCR determines whether any differences in user interface design between the generic combination product as compared to the RLD are acceptable. Specifically, DCR assesses comparative analyses submitted in an ANDA and determines whether there are minor design differences and/or other design differences, and if DCR identifies other design differences, they determine whether additional information and/or data are needed to demonstrate whether the differences in design impact the clinical effect and safety profile of the generic combination product when compared to the RLD. DCR consults DMEPA on comparative analyses as needed and on all CUHF study protocols and results. DCR also participates in regularly scheduled meetings with DTP I and DMEPA to support shared learning, awareness, and consistency in the assessment and characterization of user interface differences for combination products submitted under different application pathways.
 - **OSE's Divisions of Medication Error Prevention and Analyses (DMEPA):** DMEPA reviews CUHF study protocols. Upon consultation, DMEPA reviews results from CUHF studies submitted in an ANDA and responds to consults from DTP I and DCR on comparative analyses or questions where DMEPA's expertise can inform the review. DMEPA also participates in regularly scheduled meetings with DTP I and DCR to support shared learning, awareness, and consistency in the assessment and characterization of user interface differences for combination products submitted under different application pathways.
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PROCEDURES

1. Responding to inquiries from prospective applicants in pre-submission controlled correspondence and pre-ANDA meetings regarding the user interface of a generic combination product:
 - a. DTP I assesses the comparative analyses and determines whether there are minor design differences and/or other design differences.⁶

⁶ DTP I consults DMEPA on comparative analyses as needed. DTP I may, for example, consult DMEPA to respond to inquiries in cases where OGD determines that DMEPA's medication and use error prevention or human factors expertise may be appropriate.

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- b. If DTP I identifies other design differences, and additional data and/or information may be warranted, they communicate to the prospective applicant recommendations on how they may be able to address the differences.
 - c. If the prospective ANDA applicant responds to DTP I's recommendations by submitting a proposed CUHF study protocol or submits questions regarding a proposed protocol for a CUHF study in a pre-submission controlled correspondence or a pre-ANDA meeting request, DTP I consults DMEPA.⁷
 - d. If a prospective ANDA applicant submits results from a CUHF study and the applicant requests confirmation that the study adequately addresses the other design differences, DTP I advises the applicant that those CUHF results cannot be reviewed in a pre-submission controlled correspondence or pre-ANDA meeting and they should instead be submitted as part of the original ANDA submission.
2. Assessing the user interface of a generic combination product in an ANDA:
- a. DCR assesses the comparative analyses and determines whether any differences in user interface design between the generic combination product and RLD are acceptable.⁸
 - i. DCR determines whether there are minor design differences and/or other design differences.
 - ii. If DCR identifies other design differences, they determine whether additional information and/or data are needed to support a determination that the differences do not impact the clinical effect and safety profile of the generic combination product when compared to the RLD. If appropriate, DCR issues a deficiency with recommendations on ways the applicant may be able to address the differences.
 - b. If the ANDA applicant responds to DCR's recommendations by submitting a proposed CUHF study protocol or results from a CUHF study, DCR consults DMEPA.

⁷ DTP I and DMEPA will agree on timelines for consult responses to meet Generic Drug User Fee Amendments (GDUFA) timelines.

⁸ DCR consults DMEPA on comparative analyses as needed. DCR may, for example, consult DMEPA to respond to inquiries in cases where OGD determines that DMEPA's medication and use error prevention or human factors expertise may be appropriate.

3. Meetings between DTP I, DCR and DMEPA:

- a. DTP I, DCR, and DMEPA hold regular, recurring meetings to support shared learning, awareness, and consistency in the assessment and characterization of user interface differences for combination products submitted under different application pathways.⁹
- b. DTP I, DCR, and DMEPA rotate which division schedules and develops the agenda for each meeting. The division developing the agenda requests meeting topics from the other divisions prior to the meeting.

REFERENCE

- Draft guidance for industry, *Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA* (Jan. 2017).

EFFECTIVE DATE

- This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

| Effective Date | Revision Number | Revisions |
|----------------|-----------------|-----------|
| 6/7/2022 | N/A | Initial |
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⁹ Other OGD and OSE staff may be invited to these meetings, as appropriate.