
POLICY AND PROCEDURES

OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY
Procedures for DMEPA Intra-Center Consult to DMPP on Patient-Oriented Labeling Submitted with Human Factors Validation Study Protocols

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PURPOSE

This MAPP describes the process for the Division of Medication Error Prevention and Analysis (DMEPA) in the Office of Medication Error Prevention and Risk Management (OMEPRM), Office of Surveillance and Epidemiology (OSE) and the Division of Medical Policy Programs (DMPP) in the Office of Medical Policy Initiatives (OMPI), Office of Medical Policy (OMP) to follow when DMEPA consults DMPP for review of patient-oriented labeling¹ for drug products^{2,3} that are intended for use by patients, caregivers, or both. This MAPP applies to proposed patient-oriented labeling submitted as part of human factors (HF) validation study protocols evaluated under the jurisdiction of the Center for Drug Evaluation and Research (CDER) or consulted to CDER from the Center for Biologics Evaluation and Research (CBER).

This MAPP fulfills a PDUFA VI performance goal of ensuring the efficient, effective, and consistent combination product development and review as it relates to patient-oriented labeling, including instructions for use materials, for those drug-device and biologic-device combination products regulated by CDER and CBER.⁴

¹ For the purposes of this MAPP, patient-oriented labeling refers to FDA-approved patient instructional materials, specifically Instructions for Use (IFUs) and Quick Reference Guides (QRGs).

² For the purposes of this MAPP, drugs refers to drugs and biologics regulated in Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER). This MAPP does not apply to drug-device combination products submitted under an abbreviated new drug application.

³ This includes combination products. See definition in 21 CFR 3.2. For the purposes of this MAPP, we are referring to combination products whose jurisdiction falls within CDER and CBER.

⁴ PDUFA VI reauthorization performance goals and procedures for fiscal years 2018 through 2022, Section I.I.5.c.iii available at <http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM511438.pdf>

BACKGROUND

DMEPA holds primary responsibility for the review of HF submissions for NDAs and BLAs. During the product development, sponsors⁵ often contact the agency for advice regarding product design and HF validation studies. These interactions can begin early in development (e.g., the pre-IND process) and continue through the post-approval period, when modifications to products are made. During product development, sponsors may submit HF validation study protocols and associated labels and labeling, including patient-oriented labeling, for Agency review and comment prior to initiating HF validation studies.

When patient-oriented labeling is part of a HF validation study protocol, DMEPA will consult DMPP for an expert review of the patient-oriented labeling and then send sponsors a single set of recommendations that includes recommendations from both divisions.

POLICY

1. The OSE SRPM, and all reviewers within DMEPA and DMPP, will follow this process to provide a single set of labeling recommendations to the sponsor during review of the HF validation study protocol.
2. DMEPA and DMPP will meet the agreed upon due dates and timeframes necessary to achieve program goal dates.
3. Discussions and decisions will be made in accordance with CDER's policies on equal voice, differing professional opinions, and if necessary, dispute resolution.⁶

RESPONSIBILITIES

OSE DMEPA Safety Evaluator (SE) will:

- Identify the need for and work with the OSE SRPM to issue an intra-center consult to DMPP to review patient-oriented labeling submitted with HF validation study protocols.

⁵ For purposes of this MAPP, unless otherwise specified, persons responsible for making submissions are referred to as sponsors.

⁶ See MAPP 4151.1, Scientific / Regulatory Dispute Resolution for Individuals Within a Management Chain, version 10/12/10, MAPP 4151.2, Resolution of Differing Professional Opinions: Review by Ad Hoc Panel and CDER Director, version 10/12/10 and MAPP 4151.8, Equal Voice: Discipline and Organizational Component Collaboration in Scientific and/or Regulatory Decisions, version 09/16/10.

- Evaluate the HF validation study protocol.
- Work with the DMPP reviewer to resolve any conflicts between the DMEPA HF validation study protocol review and the patient labeling review.
- For HF validation study protocols evaluated for CDER-regulated products, create a single set of recommendations that includes DMPP patient labeling recommendations that will be subsequently sent by the OSE SRPM in a Human Factors General Advice Letter (see OSE SRPM responsibilities below).
- For HF validation study protocols evaluated for CBER-regulated products, send a single set of recommendations that includes HF validation study protocol recommendations and patient-oriented labeling recommendations (including DMPP patient labeling recommendations) to CBER. CBER then communicates the overall recommendations to the sponsor.

OSE Safety Regulatory Project Manager (SRPM) will:

- Serve as the point of contact for DMPP during the review.
- Serve as the sponsor's point of contact for HF submissions for CDER-regulated products (NDAs and BLAs).
- Work with DMEPA to send consults to DMPP.
- For HF validation study protocols evaluated for CDER-regulated products, prepare a Human Factors General Advice Letter that includes HF protocol recommendations and patient-oriented labeling recommendations from DMEPA and DMPP, and sends it to the sponsor.

OMP DMPP Reviewer will:

- Review patient-oriented labeling and respond to the intra-center consult from DMEPA by the requested due date and communicate delays, if any, prior to the due date.
- Work with the DMEPA staff to resolve any conflicts between the patient labeling review and the DMEPA HF validation study protocol review.

PROCEDURES

Consult Initiation (OSE/DMEPA)

1. When OSE receives a HF validation study protocol as part of a submission or consult to CDER, the OSE SRPM creates an assignment to DMEPA in the CDER document archiving system.
2. DMEPA evaluates the HF validation study protocol submission to determine if it includes patient-oriented labeling.
 - a. If this labeling is included, DMEPA asks the OSE SRPM to issue an intra-center consult request to DMPP using the Patient Labeling Consult Request Form.
 - b. The OSE SRPM will:
 - i. Serve as the point of contact for DMPP during the consult review if clarification is needed about the consult or additional information is needed from the sponsor.
 - ii. Send a link to the Word version of the IFU with the consult form to DMPP. If a Word version is not available in the submission, the OSE SRPM requests it from the sponsor.
 - iii. Notify the Office of New Drugs (OND) Division RPM of the the consult to DMPP.

Consult Receipt and Review (DMPP)

1. When DMPP receives the Patient Labeling Consult Request from DMEPA, DMPP will assign the consult to a DMPP reviewer.
2. The DMPP Project Manager will notify the OSE SRPM and DMEPA reviewer of the assigned DMPP reviewer.
3. DMPP will complete their review of the patient oriented labeling and upload the review to the CDER document archiving system.^{7,8}
4. Once finalized in the document archiving system, DMPP will send Word versions of their patient labeling consult review and track-changed patient-oriented labeling to the DMEPA reviewer and OSE SRPM.

⁷ In the DMPP consult review, the review notes that DMPP labeling recommendations will be incorporated into the Human Factors General Advice Letter.

⁸ In instances where DMEPA is consulted by CBER for review of a HF validation study protocol with patient-oriented labeling, instead of uploading the DMPP review to the CDER document archiving system, DMPP will provide DMEPA with electronically signed PDF and Word versions of their consult review and track-changed patient-oriented labeling to share with CBER.

Integration of Labeling Recommendations in Human Factors General Advice Letter

1. DMEPA will complete their review of the HF validation study protocol submission.
2. If the DMEPA SE has any questions concerning the completed DMPP patient-oriented labeling review, they will contact the DMPP reviewer to discuss and reach alignment.
 - DMEPA and DMPP staff should discuss and seek to reach scientific agreement in a timely manner.⁹
3. DMEPA will reference the DMPP consult review in DMEPA's HF validation study protocol review.
4. DMEPA shares recommendations for the HF validation study protocol with the respective OND Review Division to determine if any factors have been identified by OND which may impact the recommendations.
5. DMEPA's HF validation study protocol review is finalized and placed into the CDER document archiving system¹⁰:
 - DMEPA notifies appropriate DMPP individuals through CDER's document archiving system, including at minimum, the Project Manager, reviewer, and team leader when their review is finalized.
6. The OSE SRPM prepares the Human Factors General Advice Letter which includes a single set of recommendations for the HF validation study protocol and patient-oriented labeling.
7. The DMEPA Division Director or designee is the signatory authority for the Human Factors General Advice Letter, which is sent to the sponsor.
 - The OSE SRPM will notify CDER-DMPP-Patientlabelingteam@fda.hhs.gov through CDER's document archiving system when the Human Factors General Advice Letter is finalized.

⁹ MAPP 4151.8 Equal Voice: Discipline and Organizational Component Collaboration in Scientific and/or Regulatory Decisions, version 09/16/10
<http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/UCM229014.pdf>

¹⁰ In instances where DMEPA is consulted by CBER for review of a HF validation study protocol with patient-oriented labeling, DMEPA will send CBER the DMEPA HF validation study protocol review, DMPP consult review, and track-changed patient-oriented labeling, which will be entered by CBER into their document archiving system. DMEPA will carbon copy the OSE SRPM and DMPP reviewer on the communication to CBER. CBER will communicate HF validation study protocol recommendations and patient-oriented labeling recommendations to the sponsor.

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8. If questions from OND, CBER, or the sponsor arise regarding the patient-oriented labeling recommendations before or after reviews are finalized, DMEPA and DMPP will jointly work on responses to questions.
 9. Based on recommendations received, if the sponsor submits revised patient-oriented labeling for Agency review or comment, DMEPA will issue a new consult to DMPP.

REFERENCES

- MAPP 4151.8 Equal Voice: Discipline and Organizational Component Collaboration in Scientific and/or Regulatory Decisions, version 09/16/10
<http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/UCM229014.pdf>
- MAPP 4151.1, Scientific / Regulatory Dispute Resolution for Individuals Within a Management Chain, version 10/12/10
<https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/UCM073557.pdf>
- MAPP 4151.2, Resolution of Differing Professional Opinions: Review by Ad Hoc Panel and CDER Director, version 10/12/10
<https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/UCM073558.pdf>

EFFECTIVE DATE

This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
	N/A	Initial