POLICY AND PROCEDURES

OFFICE OF NEW DRUGS

NDAs and BLAs: Filing Review Issues

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PURPOSE

- This MAPP establishes procedures for identifying review issues during the filing review of all original new drug applications (NDAs), original biologics license applications (BLAs), and efficacy supplements within the Center for Drug Evaluation and Research (CDER) and outlines the procedures for informing the applicant about these issues. It does not apply to labeling supplements that contain clinical data.

BACKGROUND

- On June 12, 2002, the President signed the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, which includes the Prescription Drug User Fee Amendments of 2002. In conjunction with the June 2002 reauthorization of the Prescription Drug User Fee Act (PDUFA), the Food and Drug Administration (FDA) agreed to meet specific performance goals (PDUFA Goals). The PDUFA Goals outline the basic requirements for first cycle review performance, including applicant notification of issues identified during the filing review.

- The June 2002 reauthorization of PDUFA performance goals directed the FDA to "report substantive deficiencies identified in the initial filing review to the

sponsor by letter, telephone conference, facsimile, secure e-mail, or other expedient means."

POLICY

- Any filing review issues identified during the filing review will be communicated to the applicant no later than 14 calendar days after the 60-day filing date.

- If the review team does not identify any filing review issues, the applicant will be informed of this fact no later than 14 calendar days after the 60-day filing date.

- This MAPP applies only to original NDA applications, original BLA applications, and original efficacy supplements. It does not apply to labeling supplements that contain clinical data.

RESPONSIBILITIES

Review Team Members will:

- Identify any potential filing review issues during the filing review and inform the other members of the review team about these issues at or before the filing meeting.

- For each filing review issue, determine whether to request a response from the applicant.

Team Leaders; Chiefs, Project Management Staff; and Review Division Directors will:

- Provide guidance to the review team about identifying potential filing review issues and distinguishing any internal review discussion points that do not meet the definition of filing review issues.

- Determine the appropriateness of the filing review issues to be conveyed to the applicant.

Review Division Project Management Staff will:

- Convey and/or confirm conveyance of filing review issues, or lack thereof, to the applicant within the designated time frame, including standard language on the preliminary nature of these findings.

- Document in writing conveyance of filing review issues, or lack thereof, to the applicant.

PROCEDURES

- **Identification of Filing Review Issues:** During the initial filing review of a newly submitted original NDA, original BLA, or efficacy supplement, any issues that may meet the definition of a filing review issue should be identified and discussed within the review team (e.g., at a 45-day filing meeting). Following discussion with the entire review team, if filing review issues are identified for multiple review disciplines, the chief, project management staff, or review division director should authorize communication of that information to the applicant. If all filing review issues pertain to only one review discipline, the relevant review discipline team leader can authorize this communication. The review team can request a response from the applicant on any number or none of the identified issues.

- **Communication of Filing Review Issues to Applicant:** All filing review issues identified by the review team will be conveyed to the applicant in a single communication, which will include the FDA's expectations for applicant responses, if any. This communication may be by letter, telephone conference, facsimile, secure e-mail, or other expedient means and should be made within the specified time frame.

- **Documentation of Filing Review Issues:** Communication of filing review issues to the applicant will be documented in writing and archived using standard CDER processes.

REFERENCES

1. *PDUFA Reauthorization Performance Goals and Procedures*, an enclosure to a letter dated June 4, 2002, from the Secretary of Health and Human Services, Tommy Thompson, to Congress, available at https://wayback.archive-it.org/7993/20170723022010/https://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm118928.htm

2. MAPP 6025.4 *Good Review Practice: Refuse to File* (https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/default.htm)

3. Draft guidance for industry *Refuse to File: NDA and BLA Submissions to CDER*[1] (https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm)

DEFINITIONS

- **Filing review issues:** Substantive deficiencies or concerns identified by the review team during the initial filing review for an NDA, BLA, or efficacy supplement that appear to have been inadequately addressed in the application and merit particular attention during the review process. These issues may have significant impact on the FDA's ability to complete the review of the application or approve the application or parts of the application. Filing review issues are distinct from application deficiencies that serve as the basis for a refuse-to-file action. Filing review issues pertain only to applications that have been filed.

EFFECTIVE DATE

This MAPP is effective upon date of publication.

[1] When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA Drugs guidance Web page at https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.