POLICY AND PROCEDURES

OFFICE OF NEW DRUGS

Classifying Resubmissions of Original NDAs, BLAs, and Efficacy Supplements in Response to Complete Response Letters

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PURPOSE

This Manual of Policies and Procedures (MAPP) describes how the Office of New Drugs (OND) in the Center for Drug Evaluation and Research (CDER) classifies resubmissions of original new drug applications (NDAs), original biologics license applications (BLAs) for originator biological products and related biological products, and efficacy supplements to NDAs and BLAs for originator biological products and related biological products, received in response to complete response letters as Class 1 or Class 2 resubmissions.

BLAs and supplemental BLAs for biosimilar biological products submitted for licensure under section 351(k) of the Public Health Service Act (PHS Act) are outside of the scope of this MAPP.

Resubmissions of labeling, manufacturing, and risk evaluation and mitigation strategy (REMS) supplements do not receive the Class 1 or Class 2 distinction and are outside of the scope of this MAPP.

BACKGROUND

- As referenced in the Prescription Drug User Fee Act of 1992 (PDUFA), the Food and Drug Administration (FDA) committed to user fee performance goals, including the goal of reviewing and acting on an applicant's resubmission of an original application in 6 months or less.

- In the November 1997 letter to Congress regarding the reauthorization of PDUFA, the Secretary of Health and Human Services committed the FDA to recognizing two classes of resubmissions: Class 1 and Class 2.

- Resubmissions receive their classification based on the information in the action letter response. The two classes of resubmissions have different performance goals, based on the resubmission date and the fiscal year. Performance goals are codified under 21 CFR 314.110.

- Applications for which an action has been taken are considered filed. For this reason, no filing determination is made for resubmissions.

POLICY

- The review team and OND Clinical division director will determine whether the resubmission constitutes a complete response that addresses all deficiencies in the complete response letter. If so, the review team and the OND Clinical review division director classify the resubmission as Class 1 or Class 2. (See DEFINITIONS section for the differentiations between Class 1 and Class 2 resubmissions.)

- The OND Office of Regulatory Operations (ORO) Project Management Staff issues a letter to the applicant within 30 calendar days, acknowledging receipt of the resubmission.

  – If OND determines the resubmission is a not complete response addressing all deficiencies in the complete response letter, OND informs the applicant in the letter. The review clock does not start until the complete response is received.

  – If OND determines the resubmission constitutes a complete response, their letter states the classification, and provides the due date for action.

- The review team completes the review and acts on Class 1 resubmissions within 2 months of the receipt date.

- The review team completes the review and acts on Class 2 resubmissions within 6 months of the receipt date.

PROCEDURES

The Review Team and OND Clinical Division Director:

- Determines whether the resubmission is a complete response, addressing all deficiencies identified in the complete response letter.

- Determines the classification of the resubmission.

- Completes the review and act on all Class 1 resubmissions in two months and Class 2 resubmissions within 6 months of the receipt date.

ORO Project Management Staff:

- Upon receipt of the resubmission, consults with the review team and OND Clinical review division director to determine if the resubmission is a complete response. If so, determine the classification of the resubmission.

- Ensures the resubmission in the electronic archive is correctly coded, indicating either complete response or incomplete response.

- If the resubmission is not a complete response, sends the applicant an acknowledgment of incomplete response to an action letter.

- If the resubmission is a complete response, sends the applicant an acknowledgment of receipt letter stating the classification of the resubmission and the review goal date.

- Issues an acknowledgement letter to the applicant within 30 calendar days of receipt of the resubmission.

REFERENCES

- Prescription Drug User Fee Act (PDUFA)
- Public Health Service Act
- 21 CFR 314.110, Complete response letter to the applicant

DEFINITIONS

- **Resubmission**: A submission to an NDA, BLA, or efficacy supplement that purports to answer the deficiencies that need to be addressed by the applicant before approval as set forth in the complete response letter.

  – **Class 1 Resubmission**: A resubmission that includes one or more of the following items:

- Final printed labeling
- Draft labeling
- Safety updates submitted in the same format, including tabulations, as the original safety submission with new data and changes highlighted (except when large amounts of new information, including important new adverse experiences, not previously reported with the product are presented in the resubmission)
- Stability updates to support provisional or final dating periods
- Discussions of postmarketing requirements/commitments, including proposals or protocols for such requirements/commitments
- Assay validation data
- Final release testing on the last 1 to 2 lots used to support approval
- A minor re-analysis of data previously submitted to the application (determined by CDER as fitting the Class 1 category)
- Other minor clarifying information (determined by CDER as fitting the Class 1 category)
- Changes to a Risk Evaluation and Mitigation Strategy (REMS) that do not include Elements to Assure Safe Use (ETASU) and minor changes to REMS with ETASU

– **Class 2 Resubmission**: A resubmission that includes any item not specified as a Class 1 item, including:

- Any item requiring a presentation to an advisory committee.
- A resubmission requiring a reinspection.
- A resubmission including a REMS with ETASU not included in the original application, or significant amendment to a previously submitted REMS with ETASU.

- **Review Team**: Typically includes ORO staff, primary and secondary reviewers (e.g., clinical, clinical microbiology, biostatistics, clinical pharmacology, pharmacology/toxicology, and product quality), cross-discipline team lead (CDTL), OND Clinical review division director or deputy division director, and

any Office of Surveillance and Epidemiology (OSE) and Office of Product Quality (OPQ) representatives. Additional disciplines may be included as needed.

EFFECTIVE DATE

- This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
05/01/1998	N/A	N/A
11/07/2007	Rev. 1	
02/26/2015	Rev. 2	The time frames for completing the review of Class 1 and Class 2 resubmissions were specified as 2 months and 6 months, respectively, per 21 CFR 314.100; the time frame for issuing an acknowledgment letter was changed from 14 days to 30 days; language was added to clarify that a filing determination is not made for resubmissions; minor editorial changes were made to make clearer the process for determining whether a resubmission constitutes a complete response that addresses all the deficiencies in the complete response letter.
10/22/2024	Rev. 3	Updated to align with current OND organizational structure, any applicable user fee agreements (UFA) commitments, and contemporary CDER workflow procedures and best practices.