POLICY AND PROCEDURES

OFFICE OF NEW DRUGS

NDAs and BLAs: Communicating Target Dates Regarding Labeling, Anticipated Postmarketing Requirements (PMRs) and 506B Postmarketing Commitments (PMCs) to Applicants

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PURPOSE

- This MAPP establishes procedures for informing applicants of the target dates for communicating comments and feedback for labeling and anticipated postmarketing requirements (PMRs) and 506B postmarketing commitments (PMCs) for original new drug applications (NDAs), biologics license applications (BLAs), and efficacy supplements submitted to the Center for Drug Evaluation and Research (CDER).[1]

BACKGROUND

- On September 30, 2022, the President signed the FDA User Fee Reauthorization Act of 2022. Title I of the FDA User Fee Reauthorization Act reauthorized the Prescription Drug User Fee Act of 1992 (PDUFA). In conjunction with the

[1] 506B PMCs are studies or trials an applicant has agreed to, in writing to conduct concerning a product's clinical safety, clinical efficacy, clinical pharmacology, or nonclinical toxicology. In this MAPP, the term "PMC" refers to 506B PMCs which are reportable on the FDA's *Postmarket Requirements and Commitments* website: https://www.accessdata.fda.gov/scripts/cder/pmc/index.cfm. This MAPP does not apply to CMC PMCs which are not reportable under 506B, which are studies regarding a product's chemistry, manufacturing, and controls.

reauthorization of PDUFA, the Food and Drug Administration (FDA) agreed to meet specific performance goals. The goals are described in the commitment letter, *PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2023 Through 2027 (PDUFA VII)*. Under the PDUFA VII goals, CDER agreed to notify applicants of anticipated PMRs for new molecular entity (NME) NDAs under section 505(b) of the Food, Drug, and Cosmetic Act (FD&C Act) and original BLAs under section 351(a) of the Public Health Service Act (PHS Act).

- The President also reauthorized the Biosimilar User Fee Act (BsUFA). With this action, the Food and Drug Administration (FDA) agreed to meet specific performance goals. These goals are described in the commitment letter, *BsUFA Reauthorization Performance Goals and Procedures Fiscal Years 2023 Through 2027 (BsUFA III)*.[2] Under the BsUFA III goals, CDER must notify applicants of target dates for communicating feedback on proposed labeling and anticipated PMRs or PMCs for biosimilar BLAs under section 351(k) of the PHS Act.

POLICY

- The performance metrics to notify applicants of anticipated PMRs 6 weeks (for priority applications) or 8 weeks (for standard applications) prior to the PDUFA action goal date apply to NME NDAs and original BLAs only. Following these target dates for communication is a best practice that may be used for application types not subject to performance metrics, including non-NME NDAs, efficacy supplements (not including "SE8" and "SE9" supplements), and biosimilar applications, including Category A-F supplements, under section 351(k) of the PHS Act. Following these target dates for communication is a best practice that may also be used for communicating PMCs.[3]

- The performance metrics to communicate with the applicant regarding proposed labeling by a specified target date apply to biosimilar BLAs under section 351(k) of the PHS Act only. Communicating with the applicant regarding proposed labeling by a specified target date is a best practice for all application types, including all NDAs, BLAs, efficacy supplements (not including "SE8" and "SE9" supplements), and biosimilar Category A-F supplements under section 351(k) of the PHS Act.

- Target dates for communicating comments and feedback on labeling and anticipated PMRs/PMCs are included in the filing communication letter for

[2] These PDUFA and BsUFA documents are commonly referred to as the "goals" letters or "commitment" letters. Throughout this MAPP, they are referred to as "commitment" letters.

[3] CDER assigns efficacy supplement type/supplement-efficacy (SE) codes. An SE8 efficacy supplement proposes a change to the product labeling other than those changes described in the other efficacy supplement categories and incorporates information into the product labeling that requires clinical data to form the primary basis of approval. An SE9 efficacy supplement provides for any chemistry, manufacturing, and controls change that requires clinical data for approval.

NDAs, BLAs, and efficacy supplements. Target dates are based on the original PDUFA/BsUFA goal date. Any changes to the target dates, after they are established, will be communicated to the applicant.

- Major amendments to the application may change target dates. See the PROCEDURES section for descriptions of scenarios in which this may occur.

  – If the PDUFA/BsUFA goal date is extended by a major amendment, the Office of New Drugs (OND) provides new target dates for communicating comments or feedback on labeling and anticipated PMRs/PMCs, as appropriate.

  – If the PDUFA/BsUFA goal date is not extended by a major amendment, the original target dates for communicating comments and feedback regarding labeling and anticipated PMRs/PMCs can be retained or new target dates can be communicated, as appropriate.

- Minor amendments do not affect target dates.

- No target dates will be communicated for applications that are filed over protest in response to a refuse-to-file decision by the FDA.

RESPONSIBILITIES

Office of Regulatory Operations (ORO) Project Management Staff

- Calculates target dates for communicating comments and feedback regarding labeling and anticipated PMRs/PMCs based on review classification (i.e., priority or standard) and PDUFA/BsUFA goal date of the application.

- Discusses the calculated target dates at the filing meeting.

- After the filing meeting, communicates target dates to the applicant in the appropriate filing communication letter.

- Sends the applicant labeling and anticipated PMRs/PMCs on or before the target dates.

- If significant deficiencies in the application preclude communication of labeling or anticipated PMRs/PMCs by the target date, notifies the applicant that deficiencies preclude communication of labeling or anticipated PMRs/PMCs. (See attachment 2).

- When a major amendment is received, notifies the applicant:

- If the amendment extends the PDUFA/BsUFA goal date.
- If the amendment will change the target dates.

Review Management

- Determines if significant deficiencies in the application preclude communication of labeling or anticipated PMRs/PMCs by the target date.
- When a major amendment is received, determines if the amendment:
  - Will be reviewed or not reviewed during the review cycle.
  - Does or does not extend the PDUFA/BsUFA goal date.
  - Will or will not change the target dates.
- This role is occupied by supervisors who oversee the work of members of the review team.

PROCEDURES

Original Communication of Target Dates

- Target dates for communicating comments/feedback on proposed labeling and anticipated PMRs/PMCs are calculated by the ORO staff based on review classification (i.e., priority or standard) and PDUFA/BsUFA goal date of the application.
- The calculated target dates are discussed at the filing meeting.
- After the filing meeting, the target dates are communicated to the applicant in the filing communication letter. (See Attachment 2.)

If Significant Deficiencies Preclude the Discussion of Labeling or Anticipated PMRs/PMCs

- If significant deficiencies in the application preclude communication of feedback on proposed labeling or anticipated PMRs/PMCs by the target date, the applicant is notified. (See Attachment 2.)

When a Major Amendment is Received

- When a major amendment is received, Review Management determines whether:
  - The application will be reviewed during the review cycle.
  - The amendment extends the PDUFA/BsUFA goal date.
  - The amendment changes the target date.
- When a major amendment extends the PDUFA/BsUFA goal date:
  - Review Management determines if revised target dates for the communication of labeling comments and anticipated PMRs/PMCs are warranted.
  - ORO staff notifies the applicant (See Attachment 1 and 2):
    - That the amendment will be reviewed
    - Of the new PDUFA/BsUFA goal date
    - Of the new target dates
- In the rare case when a major amendment does not extend the PDUFA/BsUFA goal date and will be reviewed:
  - Review Management determines if the original target dates will be retained or whether new target dates will be provided.
  - ORO staff notifies the applicant if there are new target dates (See Attachment 1 and 2).
- When a major amendment will not be reviewed:
  - The applicant is notified that the amendment will not be reviewed during this review cycle, and that the original target dates still apply (see Attachment 1 and 2).

Minor Amendments

- Minor amendments do not affect the target dates.

REFERENCES

- FDA, 1992, FDA User Fee Reauthorization Act (PDUFA) Reauthorization Performance Goals and Procedures 2023 – 2027.

- FDA, 1997, Food and Drug Administration Modernization Act (FDAMA). Section 130.
- FDA, 2003, Pediatric Research Equity Act (PREA).
- FDA, 2012, Biosimilar User Fee Act (BsUFA) Reauthorization Performance Goals and Procedures Fiscal 2023 – 2027.
- FDA, Food, Drug, and Cosmetic Act (FD&C Act).
- Public Health Service Act (PHS Act).

DEFINITIONS

506B-Reportable Postmarketing commitment (PMC): Postmarketing studies or clinical trials concerning clinical safety, clinical efficacy, clinical pharmacology, or nonclinical toxicology that applicants and the FDA have *agreed* to conduct in writing; and applicants are required to report on these PMCs in their PMR/PMC annual report (21 CFR 314.81(b)(2)(vii)(a), 21 CFR 601.70(b), and Section 506B the FD&C Act, *Reports of Postmarketing Studies*).[4]

Amendment to a pending application: Any submission providing additional information to a pending original or supplemental application.

- **Major amendment:** An amendment to a pending application that contains one or both of the following:
  - A substantial amount of new data or new information not previously submitted to or reviewed by the FDA. This may include a major new clinical safety or efficacy study report, or a proposed risk evaluation and mitigation strategy.
  - A new analysis or major reanalysis of studies previously submitted to the pending application.
- **Minor amendment to a pending application:** Any amendment not meeting the criteria for a major amendment (e.g., providing explanatory information about protocol deviations and their effect on the study results, a manufacturing site clarification, and submission of limited amounts of data inadvertently left out of a final report).

[4] Reportable 506B PMCs are listed on the FDA's *Postmarket Requirements and Commitments* website at https://www.accessdata.fda.gov/scripts/cder/pmc/index.cfm.

Anticipated postmarketing requirement (PMR)/postmarketing commitment (PMC): Any study or trial based on data received with the original submission of the application that the applicant may be required to conduct (PMR), or agrees in writing to conduct (PMC), after the approval of a marketing or licensing application.

PDUFA or BsUFA goal date (User fee goal date): The date by which an action is due on a marketing or licensing application under the time frames committed to in commitment letters associated with PDUFA and BsUFA.

Postmarketing requirement (PMR): Any study or trial an applicant is required to conduct after approval of a marketing or licensing application or a supplement, including studies or trials required under the Pediatric Research Equity Act (PREA) of 2003 and 21 U.S.C. 355B(a) (see also 21 CFR 314.55(a) and 601.27(a)), the animal efficacy rule (21 CFR 314.610(b)(1) and 601.91(b)(1)), accelerated approval under 21 U.S.C. 356(b)(2)(A) and section 506(c) of the FD&C Act (see also 21 CFR 314.510 and 601.41), and section 505(o) of the FD&C Act.

Target dates: The planned dates for initial communication of labeling comments and anticipated PMRs and PMCs. In the PDUFA VII commitment letter, this is referred to as the planned review timelines.

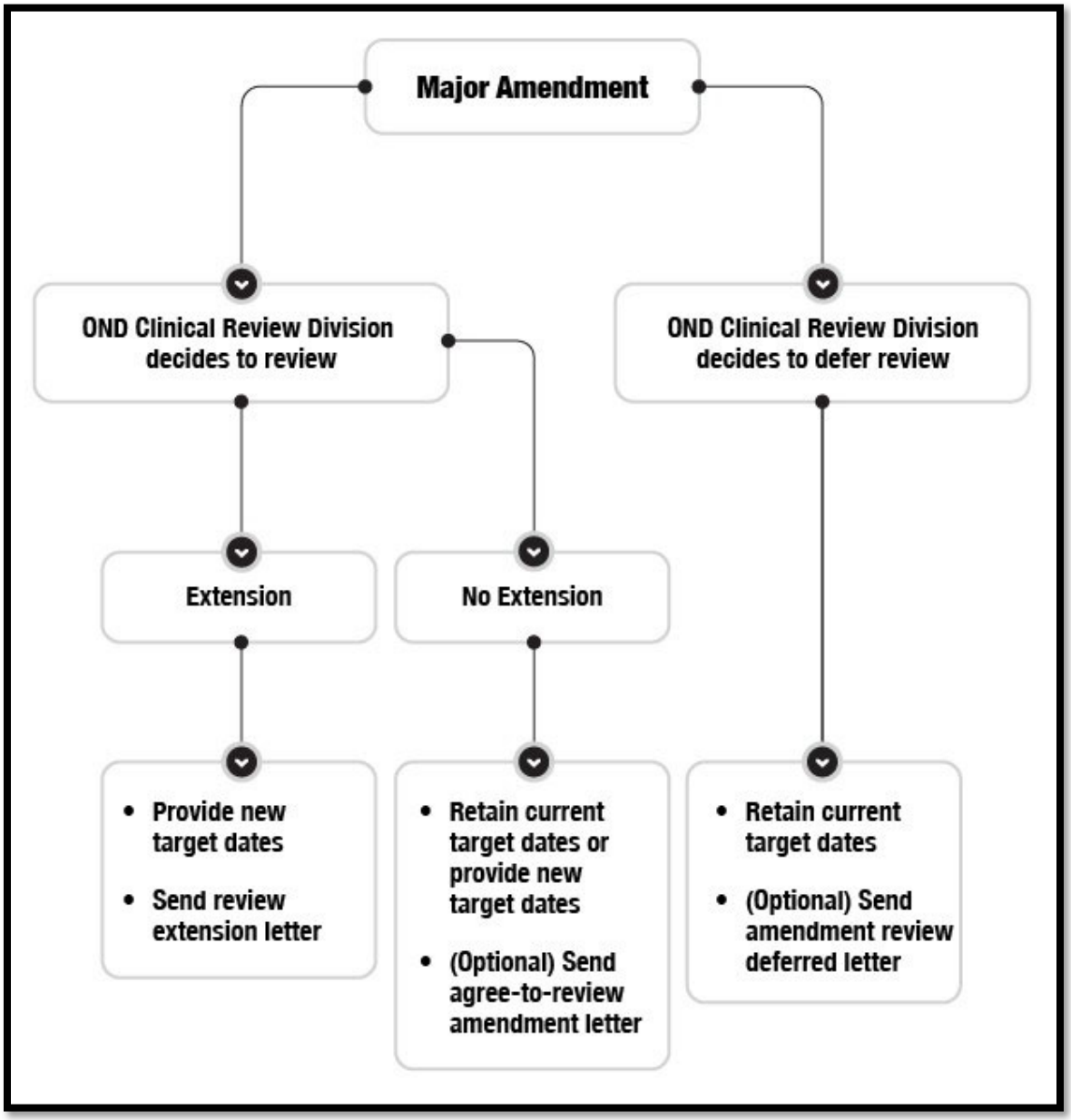
EFFECTIVE DATE

This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
6/23/2008	N/A	N/A
8/25/2014	Rev. 1	PDUFA V updates
9/19/2024	Rev. 2	Updated to align with current OND organizational structure, applicable UFA commitments, and contemporary CDER workflow procedures and best practices.

ATTACHMENT 1: Process for Major Amendments



ATTACHMENT 2: List of Standard Letter Templates for Communication of Target Dates[5]

Filing Review Issues Identified* OR *No Filing Review Issues Identified

- Use one of these letters, as applicable, to communicate to the applicant that the application is filed.
- Communicates the target dates for communication of labeling comments and anticipated PMRs and PMCs.

8-/6-Week PMR/PMC Communication Letter Template

- Use this letter to communicate anticipated PMRs/PMCs to the applicant.
- May use this letter to notify the applicant that deficiencies preclude discussion of PMRs/PMCs.
- Closes the PMR Communication goal.

Labeling Discussion Comments

- Use this letter to send initial labeling comments to the applicant.
- Closes the Labeling Discussion goal.

Deficiencies Preclude Discussion

- Use this letter to notify the applicant that deficiencies preclude discussion of labeling and PMRs/PMCs
- Closes the PMR Communication and Labeling Discussion goals.

Review Extension — Major Amendment

- Use this letter to notify the applicant that the PDUFA/BsUFA goal date is being extended.
- May extend the PMR Communication goal.
- May extend the Labeling Discussion goal.

Agree-to-Review Amendment

[5] Refer to the CDER Standard Templates (CST) Library for the appropriate letter templates.

- Use this optional letter to notify the applicant that a major amendment will be reviewed but the PDUFA/BsUFA goal date will NOT be extended.

- May retain or extend the original PMR Communication and Labeling Discussion goals.

Amendment Review Deferred

- Use this optional letter to notify the applicant that a major amendment will NOT be reviewed (the PDUFA/BsUFA goal date will NOT be extended).

- Retain the original PMR Communication and Labeling Discussion goals.