POLICY AND PROCEDURES

OFFICE OF NEW DRUGS

NDAs and BLAs: Communication to Applicants of Planned Review Timelines

Table of Contents

PURPOSE

- This MAPP establishes procedures for informing applicants of the planned review timeline, including the goal dates for discussion of labeling and postmarketing requirements (PMRs) and 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).

BACKGROUND

- On July 9, 2012, the President signed the Food and Drug Administration Safety and Innovation Act (FDASIA). Title I of FDASIA, Prescription Drug User Fee Amendments of 2012, reauthorized the Prescription Drug User Fee Act of 1992 (PDUFA). In conjunction with the reauthorization of PDUFA, the Food and Drug Administration (FDA) agreed to meet specific performance goals. These goals are described in the goals letter PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2013 Through 2017 (PDUFA V). Under the PDUFA V goals, CDER agreed to

notify applicants of planned review timelines for original NDA and BLA applications and efficacy supplements.

POLICY

- The original timeline for communication of labeling comments and draft PMRs/PMCs:
  - Will be consistent with the 21st Century Review process, taking into consideration the specific circumstances surrounding the individual application (see the CDER 21st Century Review Process Desk Reference Guide)
  - Will be based on the original PDUFA goal date
  - Will set forth the target date for communication of proposed labeling comments and draft PMRs/PMCs
- The timeline will be included in the filing communication letter for NDAs and BLAs and efficacy supplements. Any changes to the timeline, after it is established, will be communicated to the applicant by letter, telephone conference, facsimile, secure email, or other expedited means.
- Major amendments to the application may change the timeline. If the PDUFA date is extended by a major amendment, a new timeline will be provided, as appropriate. If the PDUFA clock is not extended, the original timeline can be retained or a new timeline can be communicated. (See the RESPONSIBILITIES AND PROCEDURES section for a description of situations in which this may occur.)
- Minor amendments will not affect the timeline.
- No timeline will be communicated for applications that are filed over protest in response to a refuse-to-file decision by the FDA.

RESPONSIBILITIES AND PROCEDURES

Original Timeline Communications

- The regulatory project manager (RPM) will propose timeline target dates for labeling and PMR/PMC communication based on review classification (i.e., priority or standard) of the application for discussion and concurrence during the filing meeting

- After the filing meeting, the RPM will communicate the timeline to the applicant in the filing communication letter for NDAs and BLAs (see Attachment 2)

When Significant Deficiencies Preclude the Discussion of Labeling or PMRs/PMCs

- The review team, in consultation with the Office of New Drugs division director, will determine whether significant deficiencies in the application preclude communication of labeling or PMRs/PMCs by the target date identified in the timeline

- The RPM will notify the applicant via written communication that significant deficiencies preclude the discussion of labeling or PMRs/PMCs by the target date identified in the timeline (see Attachment 2)

When a Major Amendment is Received

- The RPM, cross-discipline team leader (CDTL), and division director, in consultation with other review team members as appropriate, will determine whether an amendment to an application:

  – Is major or minor
  – Will be reviewed or not reviewed during the review cycle
  – Does or does not extend the PDUFA goal date
  – Will or will not change the timeline

- When a major amendment extends the PDUFA goal date:

  – The RPM, CDTL, and division director will determine revised target dates for the communication of labeling comments and PMRs/PMCs

  – The RPM will notify the applicant (see Attachment 2):

    - That the amendment will be reviewed
    - Of the new PDUFA goal date
    - Of the new timeline

- In the rare case when a major amendment does not extend the PDUFA goal date and will be reviewed:

  – The RPM, CDTL, and division director will determine whether the original timeline will be retained or whether a new timeline will be provided

- The RPM will notify the applicant (see Attachment 2):

  - That the amendment will be reviewed
  - That the PDUFA goal date is unchanged
  - Whether the original timeline will be retained or a new timeline will be provided

- When a major amendment will not be reviewed:

  - The RPM will notify the applicant that the amendment will not be reviewed during this review cycle and that the original timeline still applies (see Attachment 2)

Minor Amendments

- Minor amendments will not affect the timeline

REFERENCES

1. PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2013 Through 2017 (http://www.fda.gov/downloads/forindustry/userfees/prescriptiondruguserfee/ucm270412.pdf)

2. MAPP 4180.4 *NDAs/BLAs: Using the 21st Century Review Process Desk Reference Guide* (http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/default.htm)

DEFINITIONS

- **Amendment.** A type of submission that provides additional information to a pending original or supplemental application.

- **Cross-discipline team leader (CDTL).** The CDTL is the person responsible for overseeing the review of marketing applications. The CDTL works with the discipline team leaders and the RPM to ensure that scientific and regulatory issues are addressed in a timely fashion and with attention to important issues.

- **Major amendment to a pending application.** An amendment to a pending application that contains one or both of the following:

(1) A substantial amount of new data or new information not previously submitted to, or reviewed by, the FDA (e.g., a major new clinical safety or efficacy study report, a proposed risk evaluation and mitigation strategy); or

(2) 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, submission of limited amounts of data inadvertently left out of a final report).

- **Planned review timeline** (the timeline or the dates for completion of important review milestones for an application). The milestones to be communicated to the applicant that include, at a minimum, the target dates for transmitting initial labeling comments and PMRs/PMCs. The recommended timelines for communicating this information can be found in the CDER 21st Century Review Process Desk Reference Guide.

- **Postmarketing commitment (PMC).** Any study or trial that applicants have agreed to conduct after approval of a marketing or licensing application or supplement that is not a PMR.

- **Postmarketing requirement (PMR).** Any study or trial that an applicant is required to conduct after approval of a marketing or licensing application or a supplement, including studies or trials required under section 505B of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (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 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.

- **User fee goal date (PDUFA goal date).** The date by which an action is due on a marketing application under the time frames committed to in goals letters associated with PDUFA.

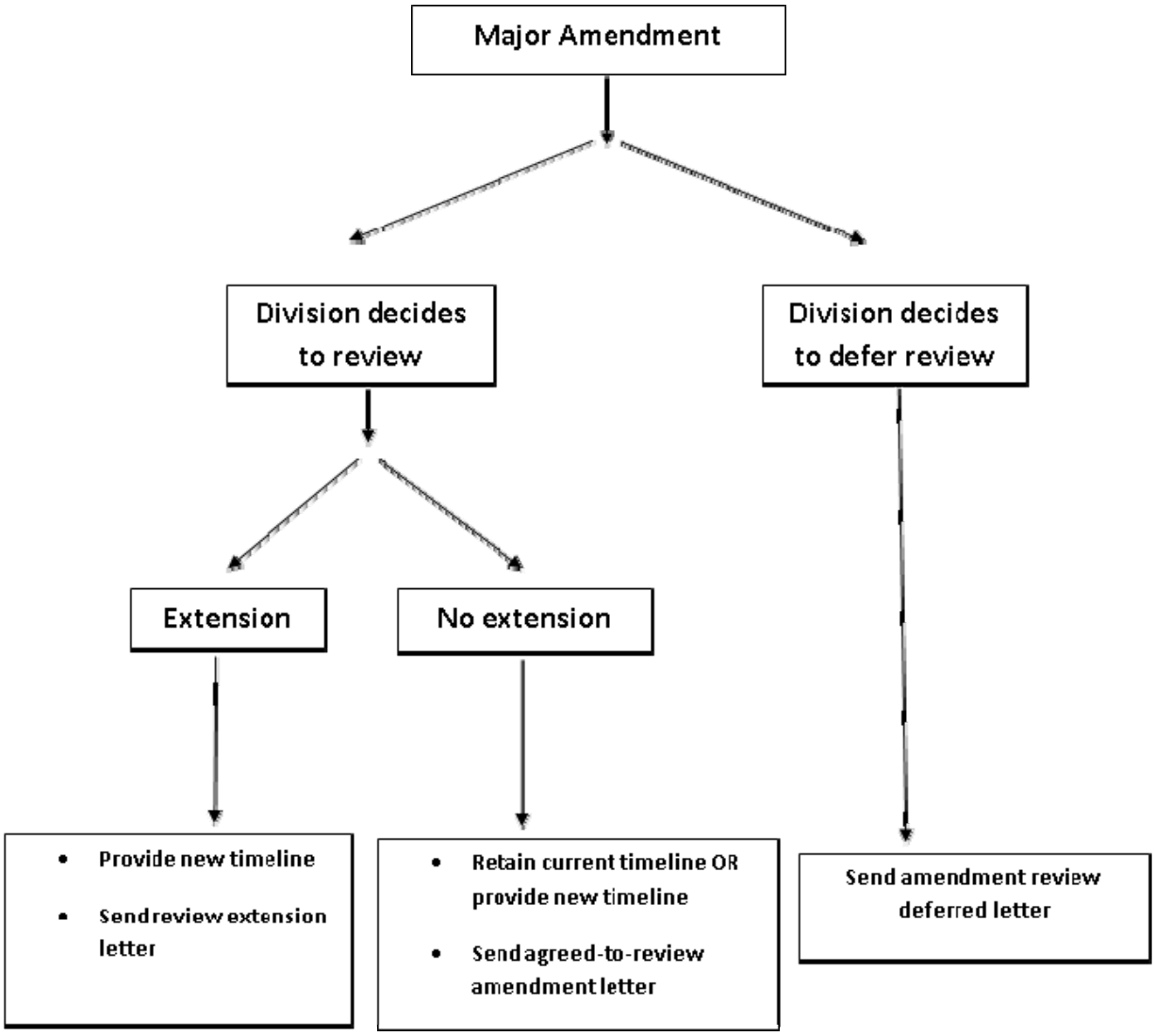
EFFECTIVE DATE

This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
6/23/08	N/A	N/A
8/25/14	Rev. 1	PDUFA V updates

Attachment 1: Timeline Process for Major Amendments



Attachment 2: Standard Letters for Communication of Planned Review Timelines

Labeling PMR/PMC Discussion Comments

- Use this letter to send initial labeling and/or PMR/PMC comments to the applicant
- Close the Planned Review Timeline Communication goal

Deficiencies Preclude Discussion

- Use this letter to notify the applicant that deficiencies preclude discussion of labeling and PMRs/PMCs
- Close the Planned Review Timeline Communication goal

Review Extension — Major Amendment

- Use this letter to notify the applicant that the PDUFA goal date is being extended
- May extend the Planned Review Timeline Communication goal

Agree-to-Review Amendment

- Use this letter to notify the applicant that a major amendment will be reviewed but the PDUFA goal date will NOT be extended
- May retain or extend the original Planned Review Timeline Communication goal

Amendment Review Deferred

- Use this letter to notify the applicant that a major amendment will NOT be reviewed (the PDUFA goal date will NOT be extended)
- Retain the original Planned Review Timeline Communication goal