
Manual of Standard Operating Procedures and Policies

License Applications

Designation of License Application Amendments as Major or Minor

SOPP 8402

Version #2

April 16, 2001

1. Purpose

This document provides guidance to CBER staff on the procedures for assigning the designation of major and minor status to amendments received within 3 months of the action due date for pending Biologics License Applications (BLA). It also describes procedures for communicating the designation to the applicant and the effect of these designations on the action due date.

This document does not address responses to action letters, including "resubmissions." <

2. Definitions

Amendment

The submission of information to an unapproved application or supplement, including additional information or reanalysis of data previously submitted, to clarify, revise or modify the application/supplement as originally submitted.

Major Amendment

An amendment to a pending **application** containing one or more of the following:

- a substantial amount of new data not previously submitted to, or reviewed by, the agency
- a substantial amount of new manufacturing or facility information not previously submitted to, or reviewed by, the agency
- a new analysis of studies previously submitted to the pending application

Note: An amendment to a **supplement** cannot be classified as a major amendment. Also, amendments received following a complete review are not considered major amendments.

Minor Amendment

Any amendment not meeting the criteria for major amendments above. Any amendment to a supplement is a minor amendment.

Unsolicited Amendment

A submission of information or data that the agency has not requested.

4. Background

In commitments made in support of the Prescription Drug User Fee Act of 1992 (PDUFA), CBER agreed to the goal of complete reviews of license applications and supplements within specified time frames. As part of the re-authorization of PDUFA [Section 103 of the FDA Modernization Act of 1997] CBER has agreed to revise the goal for complete review of a standard biologics license application or clinical efficacy supplement to 10 months. The time frame for priority applications and clinical efficacy supplements and for manufacturing supplements that do not contain clinical data and do not require prior approval will continue to be 6 months. The time frame for manufacturing supplements that do not contain clinical data but do require prior approval will become 4 months over the time of PDUFA 2. Complete review comments are communicated to the applicant in an action letter, which stops the review clock.

Other comments not constituting a complete review may be transmitted in an information request (IR) or discipline review (DR). Neither an IR nor a DR stops the review clock. Responses to an IR or DR, and unsolicited information may be received from the applicant during the review of an application or supplement. These submissions are amendments to the pending file.

Each submission to a pending application is assessed for its effect on the review clock. Receipt of a major amendment to an application within three months of the action due date will extend the action due date by three months. Minor amendments will not affect the due date. It is therefore necessary to determine whether amendments to an application received within 3 months of the action due date are **major** or **minor amendments** in order to assess their effect on the action due date.

5. Policy

All priority and standard license applications or supplements subject to the PDUFA will be reviewed within established timeframes. Non-PDUFA products will be reviewed under the managed review process adhering to the timeframes as resources permit. The results of each complete review will be communicated in the form of the appropriate action letter.

Most unsolicited amendments to applications are discouraged; however, in some cases (i.e., new adverse reaction or safety information) such amendments may be necessary. Normally, unless the amount and type of information is substantive or voluminous, the review of a clarifying IR letter response will occur during the current review cycle. A response to a DR letter conveying deficiencies identified in a discipline review may be reviewed at the Office's discretion, if the review can be completed in the current review cycle (including the extension for a major amendment). If an amendment submitted within three months of the action due date is determined to be a major amendment, the applicant will be informed of this designation and of the resulting change to the action due date. Receipt of a major amendment within three months of the action due date for an application will extend the action due date by three months.

A single extension will be granted for a major amendment to any particular application; i.e. a later

amendment cannot also be classified as a major amendment which further extends the action due date. Subsequent amendments to that application in most cases will not be reviewed until CBER receives a complete response to an action letter containing comments from the review of the original submission and the first major amendment.

This policy applies to both PDUFA and non-PDUFA products reviewed under the managed review process.

6. Responsibilities and Procedures

It is the responsibility of the Regulatory Project Manager (RPM) of the application to assure that the designation of amendments as major or minor will be made.

- The designation of a submission as a major or minor amendment should be made within 14 days of receipt.
- It is the responsibility of the RPM to make the decision in consultation with the review committee, or other individuals as needed.

CBER will not usually review an unsolicited amendment or a response to a DR received after the review of the application is complete and the issuance of an action letter is imminent (e.g., the type of action letter has been decided and comments are being drafted). The receipt of these amendments does not affect the action due date for the application. However there may be cases such as in a priority application where the amendment may support an approval in that review cycle, in which the reviewing office will determine that the information should be considered. If these amendments are to be reviewed a designation of major or minor must be made.

- Comments from the review of a major amendment will be included in the action letter.
- Amendments received after a major amendment generally will not be reviewed except as part of a complete response to an action letter. The applicant's response to the action letter may refer to this information.

If any amendment received within three months of the action due date is a major amendment, the applicant will be notified of the designation and of the new action due date in a letter sent by the Office applications division.

Major amendments will be identified as such in the Regulatory Management System - Biologics License Application (RMS-BLA) tracking system. (Refer to Office specific procedures for individuals responsible.)

Minor amendments will be listed in the RMS-BLA tracking system as amendments. (Refer to Office specific procedures for individuals responsible.)

7. Effective Date

April 16, 2001

8. History

Written By	Approved By	Approval Date	Version Number	Comment
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Application Policy Task Force	Rebecca Devine	8/1/1995	1	Reissued as SOPP 8402 in 11/21/1996. No change to Guide content. Formerly OD-R-7-96
Gilliam B. Conley Len Wilson	Robert A. Yetter, PhD	4/16/2001	2	Updated to reflect policy changes: <ul style="list-style-type: none">• BLA replaces ELA & PLA• major amendment option no longer available for supplements• current milestone time frames

Updated: April 26, 2001