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# Manual of Standard Operating Procedures and Policies

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## Regulatory - License Applications

### Complete Review and Issuance of Action Letters

SOPP 8405

Version #4

September 20, 2004

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#### 1. Purpose

The purpose of this document is to describe the policies and procedures that the Center for Biologics Evaluation and Research (CBER) staff will follow to perform complete reviews of applications and supplements and communicate deficiencies to applicants.

#### 2. Definitions

##### Complete Biologics License Application

A biologics license application will be considered complete for filing purposes if it contains all of the data and critical review elements necessary for initiating a meaningful review process. In considering the completeness of an application, CBER staff should determine whether the application contains the elements described in the Guidance for Industry on the Chemistry Manufacturing and Controls and Establishment Description Information appropriate for the product, in addition to the applicable requirements outlined in Title 21, Code of Federal Regulations (21 CFR) Sections 601.2 and 601.3 and the elements described in the CBER "Refusal To File" (RTF) [SOPP 8404](#).

##### Information Requests

Communications asking for data or information needed to complete the review of an application or supplement are information requests. They are not considered to be Action Letters because they do not represent a complete review of the submission and therefore do not stop the review clock. Information Requests can include letters, facsimiles, documented telecons, etc.

##### Priority Applications

The product, if approved by CBER or the Center for Drug Evaluation and Research (CDER), would be a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention of a serious or life-threatening disease. In addition, for drug products under CDER's jurisdiction, the product, if approved, would be a significant improvement in the treatment, diagnosis or prevention of a non-serious disease. Examples include:

- documented improvement in patient compliance

- elimination or significant reduction of a treatment-limiting drug reaction
- demonstration of safety or effectiveness in a new subpopulation of patients with the disease.

### **Standard Applications**

All non-priority applications will be considered "standard" applications.

### **Action Letters**

The following letter types constitute complete Agency actions (for performance goal and review clock purposes) in response to the application or supplement review process. Action letters are the result of complete Agency review of applications or supplements and stop the review clock.

- **Complete Response Letter**
  - This letter will be issued when the complete review indicates that there are deficiencies remaining that preclude the approval of the application or supplement at that time. The Complete Response Letter will:
    - Summarize all of the deficiencies remaining, and
    - Where appropriate, describe actions necessary to place the application/supplement in a condition for approval.
  - **Approval Letter**
    - Following completion of all aspects of the review process, including testing of submitted product lots, pre-licensing inspection and evaluation of final printed labeling or a suitable alternative, an approval letter will constitute the final action.

### **3. Background**

CBER will utilize Action Letters (i.e., complete response and approval) following each complete review cycle for biologics license applications (BLAs) and supplements. FDA committed to meeting various performance goals in support of the user fee program established by the Prescription Drug User Fee Act of 1992 (PDUFA). CBER intends to perform an initial, complete review of an application or supplement subject to user fees within the time frames contained in the FDA's June 4, 2002 letter to Congress setting out the performance goals regarding the Food and Drug Administration Modernization Act of 1997 (FDAMA), in which PDUFA (PDUFA 3) was reauthorized. CBER staff should conduct a complete review of a manufacturer's complete response to a previously issued action letter (resubmission) according to the procedures set out in [SOPP 8405.1](#).

### **4. Policy**

The Secretary's letter to Congress sets out the performance goals regarding PDUFA 3. CBER staff should review all priority and standard license applications and amendments subject to PDUFA 3 within established time frames. The results of each complete review will be communicated to the applicant via the appropriate Action Letter. The signature authorities for Action Letters issued by the various offices are contained in the Appendix of this SOPP. Additionally, as agreed during the 1993 senior management go-away, the same procedure for complete review and issuance of action letters will apply to products not subject to user fees, with the exception that strict adherence to the time lines will be recommended as resources permit but not required.

### **5. Responsibilities and Procedures**

#### **User Fee Applications**

Follow the general guidance specified below for all applications and supplements subject to user fees (on or after September 1, 1992, and not specifically exempted by the legislation).

- Designate the status of the application (i.e., priority or standard) at the time of the pre-BLA meeting or as soon as possible after receipt.
- Verify the status of all fees owed by the applicant. The User Fee Act provides that an application will not be accepted for filing unless the applicant has paid all fees due. Information regarding payment of fees will be provided to CBER in reports issued by the Office of Financial Management (OFM), FDA.
- Assign the submission tracking number when the application is received in the application division of each office and correlate the receipt of payment with the submitted application.
- Use an administrative screening procedure as an initial step to document that the submission contains all of the required filing elements (this is not an in-depth review as to the quality of the submitted data).
- Form the review committee and meet in accordance with guidance established and issued by each office.
- Make a refusal to file decision by the time of the 45-day meeting. Notify the applicant of the decision in accordance with the CBER refusal to file guidance document.
- If the application/supplement is accepted for filing, information requests may be utilized up to the time that a complete action is taken.
- The application/supplement should be acted on within the appropriate time frame. Such action consists of a complete review followed by issuance of an action letter (complete response, or approval). If information requests were utilized, the dates and status of the applicant's response to such requests should be acknowledged in the action letter.
- Other actions that may be taken include withdrawal or denial.

**Applications/Supplements not Subject To User Fees**

- Designate the status of the application as either priority or standard.
- Assign the submission tracking number when the application is received in the application division of each office.
- Use an administrative screening procedure as an initial step to document that the submission contains all of the required filing elements (this is not an in-depth review as to the quality of the submitted data). Each office will define and issue a procedure for administrative screening.
- Form the review committee and meet in accordance with guidance established and issued by each office.
- Make an RTF decision by the time of the 45-day meeting as resources permit.
- The application/supplement should be acted on within the appropriate time frame as resources permit. Such action consists of a complete review followed by issuance of an action letter (complete response or approval). If information requests were utilized, the dates and status of the applicant's response to such requests should be acknowledged in the action letter.
- Other actions that may be taken include withdrawal or denial.

**6. Appendix**

Appendix 1: [Signature Authority for Action Letters](#)

**7. Effective Date**

September 20, 2004

**8. History**

Comment/Revision	Approved By	Approval Date	Version Number	Comment
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CBER Application Policy Task Force	Michael Beatrice	11/1/1993	OD-R-1-93	Reissued as SOPP 8405 in August 1997. No change to Guide content.
Robert Yetter, PhD	Rebecca Devine, PhD	5/1/1998	8405	Revised SOPP 8405 to incorporate the action letter change specified in PDUFA 2.
Leonard Wilson	Robert Yetter, PhD	8/8/2003	3	Remove BLA inactivation option; remove outdated PLA/ELA references; update some signature authorities
Pat Padgett	Robert Yetter, PhD	9/20/2004	4	Update PDUFA information and signature authorities

Updated: September 27, 2004