

SOPP 8404.1: Procedures for Filing an Application When the Applicant Protests a Refusal to File Action (File Over Protest)

Version #1

Effective Date: January 2, 2004

1. Purpose

The purpose of this document is to describe the policies and procedures to be followed when an Applicant disagrees with a Refusal to File (RTF) action and requests that CBER file the application over protest.

2. Background

To obtain a biologics license under section 351 of the Public Health Service Act for any biological product, a manufacturer must submit an application to CBER as per 21 CFR 601.2. Within 60 days of receipt, CBER will review the license application and will determine whether the submission meets the standards established to initiate a meaningful review (See SOPP 8404, Refusal to File Guidance for Product License Applications and Establishment License Applications, Appendix 1). If the submission does not meet those standards, then, in accordance with SOPP 8404, CBER will notify the applicant that FDA refuses to file the application. A refusal-to-file action (RTF) (letter) by the Agency notifies the Applicant that (a) major deficiency/deficiencies exist(s) in the application and gives the applicant the opportunity to amend their application so that a complete review can be conducted by FDA.

An applicant may disagree with the CBER refusal to file decision and request a meeting to further discuss why the application was not filed. After the discussion, the applicant may still disagree with CBER's decision and accordingly request that CBER file and review the application over protest. In such cases, CBER will file and review the application.

This procedure was developed to promote harmonization between regulatory processes used by CBER and CDER.

3. Policy

It is the policy of CBER that when an Applicant disagrees with a refusal to file decision by CBER, the applicant will be given the opportunity to discuss the deficiencies with CBER at a meeting and, if the applicant then requests that FDA file the application, CBER will file the application in accordance with the procedure outlined below. This policy applies to PDUFA and non-PDUFA license applications.

4. Responsibilities and Procedures

1. If CBER refuses to file an application, CBER will notify the applicant in writing in accordance with CBER SOPP 8404.
2. The Applicant may submit a request for a meeting within 30 days of the date of the refusal-to-file letter to discuss the reasons for the RTF. Such meeting requests should be granted and are generally considered to be a Type A meeting in accordance with CBER SOPP 8101.1, Scheduling and Conduct of Regulatory Review Meetings with Sponsors and Applicants (Appendix 2). The applicant should be informed by the RPM (and it should be recorded in the meeting minutes) that if the applicant plans to request that CBER file the application over protest, then the applicable user fees need to be submitted. If discussion at this meeting causes CBER to reverse the RTF decision, the RPM will inform the applicant of 1) the decision reversal and 2) the new action due date. The new action due date will be the original action due date plus the number of days between the RTF decision (RTF letter) and the RTF decision reversal. The RPM will notify the Regulatory Information Management Staff (RIMS) to reactivate the submission and reset the action due date.
3. If we receive a request in writing (mail or via fax) from the Applicant within 30 days following the meeting that CBER file the application (with or without amendments to correct deficiencies), CBER will file the application over protest and notify the Applicant in writing that the application is filed.
 - CBER will not file an application when we receive the request more than 30 days after the above meeting.
 - Once the application is filed, the review of the application will be classified as standard or priority review, as appropriate, and will be reviewed as filed.
 - The filing of the Application over protest will be regarded by CBER as a new original application for user fee purposes. Therefore the applicable fee must accompany the written request to file over protest (Appendix 3).
 - The review clock will resume upon receipt of the Applicant's written request to file over protest, providing the user fee accompanies the request.
 - The Regulatory Information Management Staff (RIMS) should be contacted by the RPM to have the Application status changed from Refused to File to Filed, the dates and schedule reset, and all other necessary changes made in RMS-BLA. History of the Refuse to File action will be retained in the Detailed Summary field.
 - DCC should be notified of the application status.
 - If the application is not filed, the RPM should notify DCC (email: DCCMARKETABLE) 120 days following issuance of the RTF

letter of the status of this application for appropriate disposition of the documents.

- If the application is filed, the RPM should immediately notify DCC (email: DCCMARKETABLE) when the application is filed and that the review will continue.

4. If the applicant amends the application to address filing deficiencies prior to the request to file over protest, CBER will file and review the amended application. If no amendment is made prior to the file over protest request, CBER will file the application as originally submitted. Amendments submitted subsequent to filing may not be reviewed during the first review cycle.

5. **Effective Date**

January 2, 2004

6. **History**

| Written By | Approved By | Approval Date | Version Number | Comment |
|--|-----------------------|---------------|----------------|----------|
| Jay Eltermann Len Wilson Pat Padgett Diane Gubernot Richard Daemer RMCC | Robert Yetter, PhD | 4/8/2005 | 1 | Original |

Appendices

- [SOPP 8404: Refusal to File Procedures for Biologic License Applications](#) Effective Date: August 27, 2007
- [SOPP 8101.1: Scheduling and Conduct of Regulatory Review Meetings with Sponsors and Applicants](#)
- [Interim Guidance, Applicability of User Fees to: 1\) applications withdrawn before filing decision, or 2\) applications the agency has refused to file and that are resubmitted or filed over protest \(PDF - 108KB\)](#) Attachment F, July 12 1993