
Manual of Standard Operating Procedures and Policies

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Issuance and Review of Responses to Information Requests and Discipline Review Letters to Pending Applications

SOPP 8401.1

Version #1

Date: June 11, 2002

1. Purpose

The purpose of this document is to describe the policies and procedures for issuing and reviewing responses to Information Request and Discipline Review letters to pending applications.

2. Definitions

Information Request (IR) letter:

A letter sent to an applicant during an application review to request further information or clarification that is needed or would be helpful to complete the discipline review. An IR letter does not necessarily reflect input from upper supervisory levels (i.e., Division or Office Directors).

Discipline Review (DR) letter

A letter sent to an applicant during an application review to convey early thoughts on possible deficiencies found by a discipline review team at the conclusion of its discipline review. Generally, each discipline reviews a different section of the biologics license application (BLA) or new drug application (NDA). These disciplines include, but are not limited to, the clinical review, the chemistry, manufacturing and controls review, the non-clinical pharmacology and toxicology review, and the human pharmacokinetics and bioavailability review. A DR letter does not necessarily reflect input from upper supervisory levels (i.e., Division or Office Directors). A single DR letter may contain comments from multiple discipline reviews if it is more efficient to do so.

4. Background

Upon implementation of the Prescription Drug User Fee Act of 1992 (PDUFA 1), the Center for Biologics Evaluation and Research (CBER) and the Center for Drug Evaluation and Research (CDER) undertook to review and act on complete NDAs and BLAs within agreed upon time frames. As part of this undertaking FDA instituted the use of two types of letters, action letters and IR letters. An action letter (not approvable, approvable or approval letter) was issued after a complete review of the application. If not an approval, the action letter contained a complete list of deficiencies in the application and completed the review cycle for the application. The next review cycle (resubmission)

began when a complete response to all deficiencies listed in the letter was received by the Agency. CDER and CBER used IR letters to ask for information that would assist reviewers during the course of the review or to convey deficiencies identified in the application in advance of the issuance of an action letter. These IR letters did not stop the review clock, did not signal the completion of a review cycle, and were not used consistently across divisions or centers.

In discussions held to prepare for the reauthorization of the Prescription Drug User Fee Act (PDUFA), industry proposed that applicants be notified of any deficiencies in an NDA or BLA as early as possible after a discipline review had been completed. It was agreed that deficiencies would be communicated in a specific type of letter. The company could then begin preparing a response to the deficiencies prior to receipt of a complete review letter, thereby decreasing the response time to the Agency and potentially expediting availability of products to consumers. Although the enclosure to the PDUFA reauthorization goals letter signed by Secretary Shalala refers to these as IR letters (see Reference 1 for PDUFA documents), FDA found it to be less confusing to clearly identify these letters as a unique type of letter, the discipline review (DR) letter. The Agency will continue to use an IR letter, if needed, to request further information or clarification that is needed or would be helpful to allow completion of the review while a specific discipline review is in progress and will use the DR letter to convey early thoughts on possible deficiencies in the discipline's section of the application when a discipline review is complete.

5. Policy

It is the policy of CBER that an IR letter may be issued to request further information or clarification that is needed or would be helpful to complete the discipline review of an original BLA or NDA. A DR letter may be issued during an application review to convey early thoughts on possible deficiencies found at the conclusion of the discipline review of an original BLA or NDA. IR and DR letters do not necessarily reflect input from upper supervisory levels (i.e., Division or Office Directors), and are signed-off according to Office-specific procedures.

6. Responsibilities and Procedures

IR letters

1. When a discipline reviewer needs, or would find helpful, a clarification or additional information to complete the review, the discipline reviewer may prepare comments to be communicated in an Information Request letter.
2. The review team Regulatory Project Manager (RPM) will then prepare an IR letter based on the clarifications or additional information requested by the discipline reviewer. The letter will be circulated for signature and issuance according to office-specific procedures.

NOTE:

- IR letters are not considered to be action letters because they do not represent a complete review of the submission and therefore do not stop the user fee review clock.
- An IR letter is issued while the discipline review continues. Information requested in IR letters should be information that is necessary or would be helpful to complete the review and, as such, is intended to be reviewed during the review cycle in which the IR letter was issued (if the response is promptly received).
- Normally, unless the amount and type of information is substantive or voluminous, the review team will review a clarifying IR letter response during the current review cycle. If the response is significant in nature, the response could constitute a major amendment.

DR Letters

1. Upon completion of a discipline review, and if time permits, i.e., the issuance of a complete review

letter is not imminent, the discipline reviewer will normally prepare comments for a DR letter to be issued to the applicant.

2. The review team RPM will then prepare a DR letter based on the discipline reviewer's comments and circulate it for signature according to Office-specific procedures.

NOTE:

- A DR letter is not considered to be an action letter because it does not represent a complete review of the submission and, therefore, does not stop the review clock.
- FDA has no obligation to review information submitted in response to a DR letter during the review cycle in which the DR letter was issued. FDA may choose to review such information if it determines that such review would not adversely affect its ability to meet its PDUFA performance goal for that review cycle.
 - If the agency elects to review the response in the current cycle, the review committee will evaluate the responding amendment upon receipt to determine whether it constitutes a major amendment (see SOPP 8402) and extends the review clock..
 - If the review committee defers the review of a response, it will be reviewed during the next review cycle as part of the complete resubmission if the applicant references such response in the resubmission.

7. Effective Date

June 11, 2002

8. References

- Guidance for Industry, Information Request and Discipline Review Letters Under the Prescription Drug User Fee Act, November 2001, ([PDF - 29 KB](#))

9. History

Version 1 - First issuance of this SOPP

Comment / Revision	Approved By	Approval Date	Version Number	Comment
Leonard Wilson, RMCC	Robert Yetter, PhD	6/11/2002	1	Original Prepared to implement PDUFA commitments.

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