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# Manual of Standard Operating Procedures and Policies

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## Communication

### Investigational and Marketable Applications: Submission of Regulatory Documents to CBER

SOPP 8110

Version #1

February 6, 2003

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#### 1. Purpose

The purpose of this document is to provide guidance to staff on procedures for the submission of regulatory documents to the Center for Biologics Evaluation and Research (CBER). This guidance will aid CBER staff when responding to inquiries from applicants and sponsors who are planning to submit documents for regulatory action. Documents submitted in accordance with this guidance facilitate initial processing by the Document Control Center (DCC) and help ensure prompt delivery to the correct office.

#### 2. Background

DCC is responsible for all mail received in CBER, including regulatory and non-regulatory mail. Regulatory mail must be processed expeditiously by DCC to ensure that CBER reviewers have adequate time for review and that regulatory deadlines are met.

Delays in processing may occur when the address is incorrect, the correct submission form is not used, a cover letter is missing or the submission is not bound. Although CBER does not have regulations specifying procedures to be used for regulatory submissions, properly prepared submissions facilitate initial processing and routing for review.

#### 3. Policy

All regulatory documents are submitted to CBER through the DCC. These procedures apply to the submission of all regulatory submissions related to Investigational New Drug (IND) applications, Biologic License Applications (BLA), New Drug Applications (NDA), 510(k) Device Applications, Pre-Market Approval (PMA) Applications, Investigational Device Exemption (IDE) Applications, and Master Files (MF).

#### 4. Responsibilities and Procedures

CBER personnel verbally respond to inquiries for advice from sponsors, prospective sponsors and applicants regarding how to submit regulatory documents to CBER. It is the responsibility of all CBER personnel who receive a request for information on the submission of regulatory documents to provide the following information to sponsors, prospective sponsors and applicants.

## Submission Binding

- Regulatory submissions should be bound and submitted according to CBER [SOPP 8007](#).
  - Delays in processing will occur if:
    - submissions are not 3 hole punched
    - submissions are not submitted in an ACCO-type binder. Three-hole hard binders (notebooks) should not be used because they may open during shipping and handling by the carrier and they do not fit conveniently on most CBER shelving.
  - If submissions are received loose or inadequately bound, they may be returned to the sponsor or applicant for further handling and processing. If the submission is returned, the submission will be date-stamped when resubmitted adequately bound.

## Number of Copies

- The appropriate number of copies should be submitted.
  - BLAs, PMAs, NDAs require an original and at least two copies
  - INDs and IDEs require an original and at least two copies
  - MFs and 510(k) require an original and at least one copy
  - For other regulatory correspondence, the original and at least one copy are recommended.
- If insufficient copies are received, processing may be delayed.
  - [SOPP 8202](#) prescribes procedures for handling INDs received with insufficient copies.

## Appropriate and Accurately Completed Submission Forms

- The appropriate submission [forms](#) should be used and all entries and boxes should be completed.
  - Form FDA 356h for BLAs and NDAs
  - Form FDA 1571 for INDs
  - Form FDA 2567 or Form FDA 356h, as appropriate for labels
  - Form FDA 2253 for Advertisements and Promotional Labeling
  - CDRH Submission Cover Sheet (Form FDA-3514) is a form used voluntarily by those making submissions to CDRH. Use of this form for device submissions being made to CBER is strongly encouraged since it will facilitate timely processing of submissions by DCC.
- It is recommended that the sponsor be advised to include a cover letter that clearly identifies the type of submission, appropriate application number and any other identifying information stipulated by FDA Guidance or request. This information should be included in a "RE:" identifying statement at the top of the front page of the letter. Examples of such information (to be bolded) include:
  - RESPONSE TO CLINICAL HOLD
  - REQUEST FOR SPECIAL PROTOCOL ASSESSMENT
  - MEETING REQUEST
  - MEETING BACKGROUND PACKAGE
  - REQUEST FOR FAST TRACK DESIGNATION
- When additional copies of a previous submission are requested, the sponsor should be given and advised to include the Document Accountability and Tracking System (DATS) Log Number or Supplement or Amendment Number of the submission.

## Large Submissions

- The sponsor should be advised to contact the appropriate CBER Regulatory Project Manager (RPM) prior to submission of large applications or supplements (more than 75 total volumes including duplicates and other copies). If the RPM is not known prior to submission, the sponsor should be advised to contact the division with which they have had previous contact and discussions concerning the application.
- The RPM determines the appropriate number of review copies required in addition to the Archival copy based on the Table of Contents. A copy of the draft Table of Contents should be faxed to the

RPM as soon as it is available. Excessive numbers of additional copies not needed for reviewers should not be requested, as they require valuable storage space and additional handling and processing.

- When a large submission is expected, the RPM notifies DCC by phone or e-mail with the following information:
  - type of application
  - approximate number of volumes per copy
  - number of copies
  - approximate delivery date
  - name and phone number of sponsor or applicant contact for large applications or supplements (more than 75 total volumes)
  - routing instructions if known.
- The DCC may contact the sponsor or applicant prior to shipment to confirm dates or other details of shipment. Delivery may be requested to a different address to streamline DCC's processing, depending on the overall size of the submission.

### **Extra (Desk) copies**

- Copies labeled as "desk copies" are accountable. All such copies are received through the DCC and logged into the appropriate databases. These copies require the same handling by the DCC. Reviewers should not request that documents be sent to them directly and should discourage offers to submit "desk copies" since this can lead to confusion in document logging and tracking. Reviewers should also refuse delivery of unsolicited "desk copies", re-directing delivery to the DCC.

### **Electronic media**

The sponsor should be advised:

- To place all electronic media accompanying any paper submissions in one box and label the outside of the box, "Electronic Media inside." If multiple boxes are being sent, then all electronic media should be placed in Box 1.
- To pack media in appropriate containers and protective material packaging to prevent damage during shipment as electronic media is easily damaged if it shifts during transport.
- Electronic media should not be placed in multiple folders throughout the submission. Media are handled separately and processing will be delayed if they are inserted into many different folders.
- Individual media should be labeled with the application number, sponsor or applicant and product name or IND title and date. If necessary, label as disk 1 of 3, 2 of 3, etc.
- The appropriate form or cover letter, as described above, should be used when electronic media is being submitted without additional paper copies.

### **Packaging and labeling of shipping box/envelope**

The sponsor should be advised to:

- Address all submissions to:  
Food and Drug Administration  
Center for Biologics Evaluation and Research  
Document Control Center, HFM-99, Suite 200N  
1401 Rockville Pike  
Rockville, MD 20852-1448
- Identify the type of document enclosed on the outside label of the package: e.g. IND, BLA, NDA, 510(k), PMA, IDE, MF
- Although not required, it is helpful for applicants to include the application number (if known) that CBER has assigned to the submission.

- Submissions should be packed into appropriate boxes or envelopes for shipping and handling.
  - Boxes should be of appropriate size. Heavy boxes above approximately 45-50 pounds are not easily handled by DCC staff.
  - Heavy boxes tend to open or break during shipment and contents may be damaged and/or lost.
  - Appropriate packing material should be used in the box if necessary to prevent the contents from shifting during shipment.
- If the submission is large, volumes should be grouped by box such that a complete submission can be assembled in the least time. Review sets should be separated and the boxes marked on the outside, for example:

Archival Copy Volumes 1-10. Box 1 of 5  
 Volumes 11-20. Box 2 of 5,

Duplicate Copy Volumes 1-10. Box 1 of 5  
 Volumes 11-20. Box 2 of 5,

Copy 1 Volumes 1-10. Box 1 of 5  
 Volumes 11-20. Box 2 of 5.

- See above section on Electronic media for packaging information, if applicable.
- If more than one submission is included in the package, each submission should be clearly separated and labeled to ensure that each submission is handled separately and not inadvertently treated as one submission.

**Multiple Packages**

- Mark the outside of the box or package with the number of total packages being submitted when it is packaged into multiple units, e.g. 1 of 4, 2 of 4, etc. This should be written on the package so it is clearly visible upon receipt.

**Delivery to CBER**

- The sponsor or applicant must arrange with the carrier for "inside" delivery of all submissions.
- There is no loading dock available for document delivery at the 1401 Rockville Pike address. The DCC is located on the second floor of the building. Pallets are not permitted on the elevator; therefore boxes must be unloaded on ground level of the rear entrance and placed on a hand-truck for delivery to the second floor. Hand trucks are not permitted through the front lobby.
- All boxes and packages must pass through an x-ray machine upon arrival.
- Hours of operation for DCC are 8:00 A.M. to 4:30 P.M. Monday through Friday, except for Federal Holidays.
- If a sponsor chooses to use the U.S. Postal Service, they should be advised that mail sent in that manner is not delivered directly to the CBER DCC but is subject to intermediate delivery and handling.

**5. Effective Date**

February 6, 2003

**6. History**

Written/Revised	Approved	Approval Date	Version Number	Comment
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Jules Meisler; RMWG; RMCC	Robert Yetter, PhD	February 6, 2003	1	Original. It replaces and includes appropriate updated information from SOPP 8102, Submission of Electronic Media, issued April 30, 1997.
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Updated: February 10, 2003