

# **SOPP 8110: Submission of Paper Regulatory Applications to CBER**

Version #3

Effective Date: October 30, 2014

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## **I. 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).

## **II. SCOPE**

This SOPP 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 SOPP facilitate initial processing by the Document Control Center (DCC) and help ensure prompt delivery to the correct office.

CBER encourages the use of the Agency's Electronic Submissions Gateway for the submission of regulatory documents to CBER. Additional information on these procedures can be found on FDA's Internet web page (see references for link).

## **III. BACKGROUND**

DCC is responsible for regulatory mail received in CBER. Regulatory mail must be processed expeditiously by DCC to ensure that CBER reviewers have adequate time for review and 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.

## **IV. DEFINITIONS**

**A. Investigational and Related Applications (IRA)** - IRAs include all original and amendments for application types that CBER receives from sponsors which are tracked in CBER's Biologics Investigational and Related Applications Management System (BIRAMS) including: Investigational New Drug Applications (INDs), Investigational Device Exemptions (IDEs), Master Files (MFs), and Emergency Use Authorizations (EUAs)

**B. Marketing submission** - Marketing submissions include all original and supplemental applications/notifications that CBER receives from applicants intending to market products regulated by CBER. Marketing submissions include Biologic License

Applications (BLA) and supplements (BLS), Premarket Notifications [510(k)], Premarket Approval Applications (PMA) and supplements (PMS), Product Development Protocols (PDP), New Drug Applications (NDA) and supplements (NDS) and Abbreviated New Drug Applications (ANDA) and supplements (ANDS).

## V. POLICY

All regulatory documents are submitted to CBER through the DCC. These procedures apply to the submission of all regulatory submissions related to Investigational and Related Applications and Marketing submissions listed under Definitions.

## VI. RESPONSIBILITIES

- A. **Document Control Center** – receives and routes regulatory submissions for the Center.
- B. **CBER personnel** who receive a request for information on the submission of regulatory documents: provide the information in this SOPP to sponsors, prospective sponsors and applicants on how to submit regulatory documents to CBER.
- C. **Sponsors/applicants** – CBER recommends that sponsors/applicants refer to these procedures when submitting regulatory documents to CBER in order to facilitate the efficient processing of their submissions.

## VII. PROCEDURES

### A. Submission Preparation

1. Submission Binding - Regulatory submissions should be bound and submitted according to CBER *SOPP 8007: DCC Binding Procedures for Regulatory Documents*.
  - a. Delays in processing will occur if:
    - i. submissions are not three hole punched
    - ii. 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.
  - b. If submissions are received loose or inadequately bound, they may be returned to the sponsor/applicant for further handling and processing. If the submission is returned, the submission received date will be the date the submission is received by DCC adequately bound.

### 2. Number of Copies

- a. The appropriate number of copies should be submitted. If insufficient copies are received, processing may be delayed. *SOPP 8202: Handling IND Submitted with Insufficient Copies* prescribes procedures for handling INDs received with insufficient copies.
  - i. BLAs, PMAs, NDAs recommend an original and at least two copies
  - ii. INDs and IDEs require an original and at least two copies
  - iii. MFs and 510(k) require an original and at least one copy
  - iv. For other regulatory correspondence, the original and at least one copy are recommended.
- b. If extra copies have been sent by request of CBER staff, CBER staff should notify DCC before submission arrives.

### **3. Appropriate and Accurately Completed Submission Forms**

- a. The appropriate submission forms should be used and all entries and boxes should be completed.
  - i. Form FDA 356h for BLAs and NDAs.
  - ii. Form FDA 1571 for INDs. It would be helpful if Form FDA 1571 is included for Master Files.
  - iii. Form FDA 356h for labels.
  - iv. Form FDA 2253 for Advertisements and Promotional Labeling.
  - v. 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.
- b. It is recommended that the sponsor/applicant 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:
  - **CLINICAL HOLD COMPLETE RESPONSE**
  - **REQUEST FOR SPECIAL PROTOCOL ASSESSMENT**
  - **MEETING REQUEST**
  - **MEETING BACKGROUND PACKAGE**

- REQUEST FOR FAST TRACK DESIGNATION
  - RESPONSE TO COMPLETE RESPONSE LETTER
  - RESPONSE TO INFORMATION REQUEST LETTER
- c. When additional copies of a previous submission are requested, the sponsor/applicant should be given and advised to include the Document Accountability and Tracking System (DATS) Log Number or Supplement or Amendment Number of the submission in the cover letter.

#### **4. Pagination**

- a. CBER requests that sponsors/applicants paginate submissions from beginning to end rather than pagination in each section.

#### **5. Large Submissions**

- a. The sponsor/applicant 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/applicant should be advised to contact the division with which they have had previous contact and discussions concerning the application.
- b. 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 additional handling and processing. These additional copies will not be stored in the DCC and will be shredded within two working days of receipt.
- c. If extra copies have been sent by request of CBER staff, CBER staff should notify DCC before submission arrives so copies will not be shredded.
- d. When a large submission is expected, the RPM notifies DCC by phone or e-mail to *DCCAction* with the following information:
- type of application
  - approximate number of volumes per copy
  - number of copies
  - approximate delivery date

- Tracking number if using commercial carrier (FedEx, UPS, etc.)
  - name and phone number of sponsor/applicant contact for large applications or supplements (more than 75 total volumes)
  - routing instructions if known
- e. The DCC may contact the sponsor/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.

## **6. Electronic media**

For purposes of this SOPP, electronic media consists of disks included as part of a paper submission.

- a. The sponsor/applicant should be advised to:
- i. 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.
  - ii. 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.
  - iii. Not place electronic media in multiple folders throughout the submission. Media are handled separately and processing will be delayed if they are inserted into many different folders.
  - iv. Label individual media with the application number, sponsor/applicant and product name or IRA title and date. If necessary, label as disk 1 of 3, 2 of 3, etc.
  - v. Use the appropriate form or cover letter, as described above, when electronic media is submitted without additional paper copies.

## **B. Shipping**

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

- a. The sponsor/applicant should be advised to:

- i.** Address all submissions to:  
Food and Drug Administration  
Center for Biologics Evaluation and Research  
Document Control Center  
10903 New Hampshire Ave.  
Building 71, Room G112  
Silver Spring, MD 20993-0002

Submissions sent to any other address will result in a delay of official receipt by FDA.

- ii.** Identify the type of document enclosed on the outside label of the package: e.g. IND, BLA, NDA, 510(k), PMA, IDE, MF, pre-submission.

- iii.** 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.

- iv.** If the submission is large, volumes should be grouped by box such that a complete submission can be assembled in the least amount of 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

- v. See above section on Electronic media for packaging information, if applicable.
- vi. 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.

## **2. Multiple Packages**

- a. 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.

## **3. Delivery to CBER**

- a. The sponsor/applicant must arrange with the carrier for "inside" delivery of all submissions.
- b. Delivery by private courier or by non-FedEx or UPS commercial couriers is made through the loading dock in Building 52.
- c. All boxes and packages must pass through an x-ray machine upon arrival.
- d. Hours of operation for DCC are 8:00 A.M. to 4:30 P.M. Monday through Friday, except for Federal Holidays.
- e. If a sponsor/applicant 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.

## **C. Meeting Packages**

1. The number of meeting packages requested should be determined by CBER staff prior to submission.
2. Meeting packages submitted as part of an IRA or pending marketing submission will be processed and routed according to standard procedures. These submissions should contain FDA form 1571, FDA form 356h or a cover letter identifying the meeting package as an amendment to an application.
3. For meeting packages not associated with an IRA or pending marketing submission, all copies received in DCC will be forwarded to the addressee or office point of contact leading the meeting as identified by the cover letter.

## **D. Desk Copies and Informally Submitted Copies**

1. Copies labeled as "desk copies" are accountable regulatory submissions.
2. Desk copies received through the DCC are logged, bar-coded, and tracked in CBER's Document Accountability and Tracking System (DATS) as part of the regulatory submission. Review committee members should discourage sponsor/applicants from marking submission volumes as "desk copies." This can lead to confusion and delay submission processing.
3. Reviewers should not request sponsor/applicants to send documents directly to them. Reviewers should also refuse direct delivery of paper regulatory submissions and inform sponsor/applicants to submit through the DCC.
4. In the event a review committee member accepts an unsolicited or informally submitted document, it should be entered into the appropriate regulatory database. Marketing submissions should be entered using the "does not have DATS login ID" process. IRA documents should be sent to DCC for entry as an application amendment.

## VIII. APPENDIX

N/A

## IX. REFERENCES

A. Web links to the references below can be found in the list following the history table.

1. SOPP 8202: Handling IND Submitted with Insufficient Copies  
<http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ProceduresSOPPs/ucm063379.htm>
2. SOPP 8007: DCC Binding Procedures for Regulatory Documents  
<http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ProceduresSOPPs/ucm109596.htm>
3. Information for the Gateway  
<http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/ucm163685.htm>

## X. HISTORY



<b>Written/Revised</b>	<b>Approved</b>	<b>Approval Date</b>	<b>Version Number</b>	<b>Comment</b>
Jules Meisler, RMS	Christopher Joneckis, PhD	October 21, 2014	3	Updated address and deliver procedures
Jules Meisler, BPS	Robert Yetter, PhD	April 5, 2010	2	Updated procedures
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.