
Manual of Standard Operating Procedures and Policies

Regulatory - License Applications

Administrative Processing of Biologics License Applications (BLA)

SOPP 8401

Version #6

May 1, 2007

[\[Printable PDF of this document\]](#)

1. Purpose

This document provides policies and procedures to Center for Biologics Evaluation and Research (CBER) staff on the administrative processing of the Biologics License Application (BLA).

2. Definitions

See the [Appendix 1 for definitions](#) and [Appendix 2 for a list of abbreviations and acronyms](#) used in this SOPP.

3. Background

On October 20, 1999 the final rule "Biological Products Regulated Under Section 351 of the Public Health Service Act; Implementation of the Biologics License; Elimination of the Establishment License and Product License" was published (64 FR 56441). This final rule addressed procedures for handling of BLAs and issuance of biologics licenses for all products subject to licensure under the PHS Act, and it amended the licensing regulations in 21 CFR 601 to reflect the changes to the licensing requirement of Section 351. The final rule became effective December 20, 1999. Since then all new submissions have been handled as BLAs using Form FDA 356h in lieu of filing an Establishment License Application (ELA) and Product License Application (PLA).

4. Policy

All new marketing submissions for products subject to licensure under the PHS Act will be handled as BLAs or supplements to BLAs. The procedures in this SOPP supplement additional CBER SOPPs (see references) that describe administrative handling and review of license applications.

It is the policy of CBER that under normal circumstances product lot(s) should be available for distribution at the time of approval of the BLA or supplement. Exceptions will be made on a case by case basis.

5. Roles, Responsibilities and Procedures

Office-specific SOPPs will address any additional responsibilities of the regulatory project manager (RPM),

reviewers, and Office staff. In no case will Office-specific SOPPs be applied across the board to review committee members from other Offices.

The Division of Blood Applications (DBA), Office of Blood Research and Review (OBRR) will continue to have full administrative responsibility for BLA issues related to licensed manufacturers of blood and blood components.

I. Pre-BLA Activities

- Requests for end-of phase 2, and/or pre-phase 3 and pre-BLA meetings will be processed as amendments to the appropriate Investigational New Drug Application (IND). If no IND exists, these requests and the associated meeting summaries will be entered in the CBER Regulatory Meeting Tracking System (CRMTS) and the Pre-Application Tracking System (PTS). Offices will follow the procedures outlined in *SOPP 8114: Administrative Processing of Documents Received Prior to Submitting Investigational or Marketing Applications (Pre-Application)*.
- If the subject of the pre-BLA meeting is to address facility or Division of Manufacturing and Product Quality (DMPQ), Office of Compliance and Biologics Quality (OCBQ), issues only, DMPQ will process the request for the meeting.
- If the pre-BLA meeting request is for blood establishments, the Blood and Plasma Branch (BPB), Division of Blood Applications (DBA), Office of Blood Research and Review (OBRR) will process the request for the meeting.
- The Regulatory Project Manager (RPM) assigned to the IND or submission will be the primary contact for information on submission of the BLA and will coordinate the following pre-BLA activities.
 1. Schedules meetings in accordance with *SOPP 8101.1: Scheduling and Conduct of Regulatory Review Meetings with Sponsors and Applicants*
 - a. Ensures appropriate participation in the meeting by representatives of all review disciplines that will be involved in the review, **starting with the pre-BLA and continuing through the BLA**. Participants should include:
 1. Product and Clinical reviewers,
 2. DMPQ/OCBQ,
 3. Epidemiology and biostatistics reviewers in the Division of Biostatistics (DB), Office of Biostatistics and Epidemiology (OBE)
 4. Bioresearch Monitoring Branch (BiMo)/Division of Inspections and Surveillance (DIS)/OCBQ,
 5. Advertising and Promotional Labeling Branch (APLB)/Division of Case Management (DCM), OCBQ
 6. Electronic Submissions Coordinator (ESC) and
 7. Consult reviewer from other Offices or Centers within the Agency as appropriate.
 - b. Ensures meeting minutes are prepared
 - c. Completes a record of the meeting in CRMTS
 - d. Distributes meeting summary to FDA participants and requestor
 2. For paper BLA submissions:
 - a. Coordinates with the applicant for the correct number of copies of pertinent volumes of the BLA for all members of the review committee and consult reviewers.
 - b. Notifies CBER's Document Control Center (DCC) of the expected arrival date and size of the application.
 - c. Contacts DCC to make delivery arrangements for large submissions and supplies DCC with sponsor/applicant contact information. DCC considers a large submission to be one that exceeds a total of 50 volumes (including copies) or about 5 cubic feet.
- Office Electronic Submissions Coordinator (ESC)

1. Works with the applicant prior to submission (usually at the pre-BLA meeting) to ensure appropriate procedures and formats for electronic submissions are followed.
2. Coordinates with the pertinent electronic submission coordinators (ESCs) in DMPQ, DB, DCC, Office of Information Technology (OIT) and the Center electronic submission coordinator (CESC). All ESCs should be notified as early as possible of a potential electronic filing to ensure their readiness to process it efficiently.
3. Additional information on electronic submissions may be found at <http://www.fda.gov/cber/esub/esub.htm>

II. BLA Activities: Receipt and Processing

Form FDA 356h should be submitted with all correspondence to CBER. This information will aid in routing the submission to the appropriate division for processing.

A. Document Control Center (DCC): Receipt and Processing

1. Receives, logs in, and routes to the appropriate Office all BLAs and extra reviewer copies. DCC will route the submission based on the product name as reported by the applicant on the Form FDA 356h.
2. Electronic submissions will be processed per established procedures and the appropriate ESCs notified (See *DCC Procedure Guide 22: Procedures for Processing, Routing, and Storing Electronic Submissions*).
3. The original copy of the submission (paper and/or electronic) will be maintained in DCC as an uncirculated record copy.

B. Regulatory Project Manager (RPM): Receipt and Processing

Upon receipt of the BLA in the product Office, the RPM will perform the following where applicable:

1. Screens the BLA to confirm all the sections are present and consistent with the TOC. Notifies the applicant of inconsistencies.
 - a. Determines the User Fee status and sends a copy of the user fee cover sheet, FDA Form 3397 (PDUFA) or FDA Form 3601 (MDUFMA) to the Regulatory Information Management Staff (RIMS) per *SOPP 8406: Verification of User Fee Data Sheet and Payment*
 - b. Determines that an Environmental Assessment (EA) or request for Categorical Exclusion (CE) has been submitted. 21 CFR 24.20-25.31 requires submission for certain products. If an EA or CE was not submitted but may be needed, the RPM will consult with DMPQ.
2. Ensures all required data is entered into the Regulatory Management System – Biologics License Application (RMS-BLA) per the RMS-BLA User Guide
 - a. All reviewers, including those in DMPQ, OBE, APLB and BiMo should be listed as committee members in RMS-BLA
3. Ensures that a Submission Tracking Number (STN) is assigned and that the STN assignment letter is issued
4. Notifies all identified committee members and their supervisors in all Offices of the receipt of the BLA
5. Ensures the submission is routed to all members of the review committee and all consult reviewers
 - a. Requests additional copies from the applicant as needed
 - b. The DMPQ or BPB/DBA Reviewer will always receive a copy of the Chemistry, Manufacturing, and Controls (CMC) and Establishment Description sections
 - c. A copy of the Table of Contents (TOC) should be sent to all committee members
 - d. Consults with APLB on all patient package inserts, prescribing information, proposed proprietary names, logos, press releases, kits, and carton and container labeling per *SOPP 8001.4: Review of CBER Regulated Product Proprietary Names* and *SOPP 8412: Review of Product Labeling*.
 1. (1) Note: Advertisements and promotional materials submitted per 21 CFR

314.550 and 601.45 for accelerated approval and restricted distribution requirements should be routed to APLB/OCBQ. Including other draft promotional materials submitted voluntarily for advisory comment by the applicant.

6. Ensures a check is made with the PTS and cross-references are listed in the regulatory databases. If appropriate, the PTS number is closed and the applicant notified.

III. BLA Activities: Filing Decision

A. Review Committee: Filing Decision

1. In consultation with the BiMo representative, determines what inspection (of clinical investigators or sponsors) are necessary and appropriate
2. Each reviewer will evaluate the pertinent information in RMS-BLA for accuracy and completeness upon receipt. If there are any additions/corrections needed, the review committee member is responsible for notifying the RPM of the changes needed.
3. Each reviewer recommends the filing status to the committee chair.
4. Identifies any substantive deficiencies for communicating in the filing letter or the day 74 letter
5. Ensures all appropriate documentation is entered in RMS-BLA and either imported into the Electronic Document Room (EDR) or forwarded to the RPM in a timely manner.

B. DMPQ or BPB lead: Filing Activities

1. Determines if a pre-approval establishment inspection is required (*SOPP 8410: Determining when Pre-License /Pre-Approval Inspections are Necessary*)

C. Review Committee Chair: Filing Activities

1. Reviews the TOC and submission to make sure all applicable scientific disciplines have been requested and relevant sections of the BLA are clearly assigned for review by the committee members. (*SOPP 8401.4: Review Responsibilities for the CMC Section of Biologic License Applications and Supplements*).
2. Determines the filing status of the submission considering all review members recommendations.
 - a. Refusal to file a BLA may be based on deficiencies found in any section of the submission per *SOPP 8404: Refusal to File Guidance for Biologics License Applications* and 21 CFR 601.12.
3. Determines if an Advisory Committee meeting is necessary.

D. RPM: Filing Activities

1. Ensures changes are made if additions and/or corrections are necessary to RMS-BLA after the review committee verifies the information.
2. Ensures that the filing decision is documented and a letter is sent to the applicant

NOTE: When a decision is made to file an application, the applicant must be notified in the filing letter within 60 days of the receipt date. Potential issues may be identified in a separate "deficiencies identified" or "no deficiencies identified" letter independent of the filing letter within 14 days of the 60 day filing date. The 60 day filing date applies to either potential review issues or no potential review issues identified during the filing review. Refer to *SOPP 8401.3 Filing Action: Communication Options*, for communication procedures.

E. Electronic Integrity Reviewer: Filing Activities

1. Upon notification of the load, checks the submission for "readability," (i.e., structure, format, presence of bookmarks, hyperlink functionality, etc.) throughout the entire submission.
2. If there is a problem with the submission, the ESC, in coordination with the CESC, will contact the applicant, usually by teleconference. The RPM will usually be included in the teleconference.
3. Troubleshoots with reviewers if there is difficulty accessing files, navigation, etc

IV. BLA: Review Activities

All actions with the exception of RMS-BLA data entry and review should be accompanied by written documentation describing the decision reached, with justification as appropriate, and submitted to the license application file by each member of the review committee.

A. Review Committee: Review Activities

1. Each member will be invited to attend all meetings and is expected to attend all appropriate meetings
2. Conducts a comprehensive review of the submission including:
 - a. Identifying any issues including informational requests
 - b. Identifying issues that could prevent approval
 - c. Developing a clear plan for addressing issues including the decision to send a Discipline Review (DR), Information Request (IR), or Complete Response (CR) letter to the applicant
 - d. Provides letter ready comments/questions to the RPM
 - e. Makes any recommendations for review to go to an advisory committee
3. Reviews and concurs with all action letters for the application
4. Ensures that all appropriate documentation (review memos, telecons, etc) is entered in RMS-BLA and either imported into the EDR or forwarded to the RPM in a timely manner
5. Identifies any issues related to promotional labeling
6. Consults with APLB on all patient package inserts, prescribing information, proposed proprietary names, logos, press releases, kits, and carton and container labeling.
7. Identifies labeling content issues related to Physician's Labeling Rule (PLR) and data element coding for Structured Product Labeling (SPL).

B. Discipline reviewer: Review Activities

1. Forwards final discipline review to supervisor(s) for concurrence.

C. CMC Reviewer/Product Lead: Review Activities

1. Enters information on animal materials in the Animal Component Database (ACD) per *SOPP 8401.5: Processing of Animal Component Information Submitted in Investigational and Marketing Applications/Notifications*.
2. Determines if testing of exhibit lots submitted in support of the BLA is necessary and in collaboration with PRB, will determine the number of samples required. Communicates these requirements to the committee chair.
3. Ensures that lot release protocols and exhibit product samples have been requested for lots in support of the application per *SOPP 8408: Collaboration of CBER Offices on Issues Related to the Release of Pre-Licensing and Routing Lots*
4. Drafts a CBER Lot Release Testing Plan for committee review and Office approval by the mid-cycle review per *SOPP 8408: Collaboration of CBER Offices on Issues Related to the Release of Pre-Licensing and Routine Lots*.

D. DMPQ reviewer: Review Activities

1. Reviews the Environmental Assessment (EA).
2. Prepares and signs the Finding of No Significant Impact (FONSI) when such a finding is appropriate.
 - a. The FONSI is sent through and signed by the DMPQ Division director and the Product Division Directors. The FONSI is forwarded to the RPM for inclusion in the final action package.
3. Prepares a review memo for the categorical exclusion (CE) that takes the place of the FONSI.
 - a. The applicant must apply for and be granted a categorical exclusion from the EA. The CE memo is forwarded to the RPM for inclusion in the final action package.

E. BiMo reviewer: Review Activities

1. Issues BiMo inspection assignments consistent with the review milestones and the needs identified by the review committee
2. Reviews BiMo inspection reports, identifies any issues related to data integrity, human subject protection or other good clinical practice issues and follows up appropriately.

Communicates any issues which may have an impact on the submission to the review committee.

3. Prepares appropriate correspondence for inspected parties. With concurrence from the Bioresearch Monitoring Branch (BMB) Chief and DIS Director, issues correspondence.
4. Provides RPM with discipline review memo which summarizes the inspection results and makes a formal recommendation regarding any substantive impact on the submission under review.
5. Files domestic inspection reports and related correspondence under the IND inspection tab. For foreign inspection, CBER retains the original inspection report and exhibits, issues the inspected party the information copy of the inspection report according to the Field Management Directive (FMD) 145, and files these reports in the IND if there is one, or in the BLA if there is no corresponding IND.

F. APLB Reviewer: Review Activities

1. Prepares consult review memo for patient package insert, prescribing information, proposed proprietary names, logos, press releases, kits, and carton and container labeling for the RPM and committee chair.
2. Consult for product office on other "patient-friendly" materials, including detailed "Instructions for Use" documents
3. Consult for product office on risk management programs, including MedGuides, Informed Consent Documents, and patient education materials.

G. Product Release Branch (PRB): Review Activities

1. Notifies committee chair and CMC Reviewer(s)/Product Lead when exhibit samples and protocols have been received per *SOPP 8408: Collaboration of CBER Offices on Issues Related to the Release of Pre-Licensing and Routine Lots*.
2. Ensures that lot release protocols are under review and that testing is being performed.
3. Notifies the chair and CMC Reviewer(s)/Product Lead of any valid test failures of exhibit lots.

H. Review Committee Chair: Review Activities

1. Ensures a mid-cycle review meeting is scheduled
2. Ensures advisory committee preparation is completed
3. Collaborates with PRB early in the review process (post filing) with regard to the CMC reviewer's(s) draft Lot Release Testing Plan and recommendations on sample and test protocol submission requirements as well as identification of individuals to conduct such testing and review (see *SOPP 8408: Collaboration of CBER Offices on Issues Related to the Release of Pre-Licensing and Routine Lots*).

I. RPM: Review Activities

1. Ensures compliance status check is initiated no less than 30 days prior to approval by DVRPA, DBA, RMS, or DMPQ, when necessary, The compliance status check request is entered in RMS-BLA by the requestor.
2. Notifies the Quality Assurance Staff (QAS) and Product Release Branch (PRB)/DMPQ/OCBQ of the draft CBER Lot Release Testing Plan.
3. Schedules a mid cycle review meeting.
4. Ensures that lot release protocols and product samples have been submitted and are under review and that testing is being performed.
5. Confirms that, when required, BiMo assignments have been issued.

J. Electronic Integrity Reviewer: Review Activities

1. Ensures that all amendments submitted conform for "readability," (i.e., structure, format, presence of bookmarks, hyperlink functionality, etc.).
2. If there is a problem with the submission, the ESC, in coordination with the CESC, will contact the applicant, usually by teleconference. The RPM will usually be included in the teleconference.
3. Aid reviewers in accessing amendments.

V. BLA Activities: Communications

A. Review Committee: Communications

1. Review and concur on all action letters routed.
 - B. DBA/BPB Lead: Communications**
 1. Prepares letters for issues associated with blood and blood components only
 - a. Obtains concurrence from the BPB Branch Chief before the DBA Division Director signs.
 - C. DMPQ Lead: Communications**
 1. Prepares letters if the only issues are establishment related and a product office is administratively processing the BLA.
 - a. Requires concurrence from the DMPQ branch chief and division director and appropriate individuals in the product office before the Office Director (or designate) with product responsibility signs.
 - D. RPM: Communications**
 1. Coordinates the issuance of all letters including acknowledgement of major amendment, Information Request (IR), Discipline Review (DR), Complete Response (CR) and Approval letters in accordance with *SOPP 8405: Complete Review and Issuance of Action Letters*. Note: Approval letters are discussed under section VII.
 2. Prepares letters involving Clinical, CMC, and establishment issues that will require review and/or concurrence from the appropriate individuals in the product office and the DMPQ division director and branch chief.
 - a. IR and CR letters will be issued over the signature of the Office Director (or designate) of the Office that is administratively processing the BLA.
 - b. DR letters will be signed according to Office specific procedures.
 3. Draft letters should be circulated electronically for a 72 hour comment period to allow review by all committee members and their supervisors.
 4. CBER generated letters that have been electronically signed by the appropriate personnel and imported into the EDR do not have to be printed and sent to DCC for archiving.
 5. Ensures the appropriate data is entered into RMS-BLA.
- VI. BLA: Pre-Approval and Pre-Licensure Inspectional Activities**
- A. Review Committee: Inspectional Activities**
 1. Questions to be addressed during the inspection should be forwarded to the inspection team two weeks prior to the inspection
 2. Members of the review committee that participate in the inspection (product specialists) are required to write their portions of the inspection report and forward to DMPQ, generally within 30 days after the inspection.
 - B. DMPQ Team Member: Inspectional Activities**
 1. Takes the lead responsibility for the inspection except as specified in section VI.C. The inspection team may include both product and DMPQ reviewers from the review committee.
 2. Confirms that all inspection team members have in-date credentials. (See *SOPP 8505: Nomination and Approval of CBER Inspectors and Product Specialists Assigned to Conduct Inspections of Biological Products*).
 3. Notifies the Division of Inspections and Surveillance (DIS), OCBQ, and the Review Committee, when the inspection is scheduled or prepares an inspection waiver memo.
 4. Notifies Office of Regulatory Affairs (ORA) contact according to the appropriate compliance program guide
 5. Ensures the Establishment Inspection Report (EIR) is written and the firm's responses to FDA Form 483 are evaluated
 6. Sends inspection close-out memo and supporting documents to OCBQ/DIS.
 7. Upon completion of the inspection and resolution of any inspection issues, prepares the inspection tab for the final action package per *DCC Procedure Guide 11: Procedure for Filing Pre-license/Pre-approval Inspection Material*. The tab will include the EIR, exhibits, response(s), and the EIR close-out memorandum.
 8. A copy of the EIR should be forwarded to DIS/OCBQ.
 - C. Blood and Plasma Branch, DBA, OBRR: Inspectional Activities**

1. Takes the lead responsibility for the pre-licensure inspection for blood establishments including coordinating and leading the inspection.
2. Confirms that all inspection team members have in-date credentials.
3. Notifies DIS/OCBQ when the inspection is scheduled.
4. Coordinates and leads the inspection
5. Writes the EIR and reviews the firm's Form 483 responses
6. Sends inspection close-out memo and supporting documents to DIS/OCBQ
7. Upon completion of the inspection and resolution of any inspection issues, prepares the inspection tab for the final action package per *DCC Procedure Guide 11: Procedure for Filing Pre-license/ Pre-approval Inspection Material*. The tab will include the Establishment Inspection Report (EIR), exhibits, response(s), and the inspection close-out memorandum and the endorsement.

D. Division of Inspections and Surveillance (DIS): Inspectional Activities

1. Prepares and sends a reviewed and redacted (as necessary) copy of the EIR to the firm consistent with the approach described in ORA's FMD – 145.
2. The inspection tab of the final action package is forwarded to the RPM per *DCC Procedure Guide 11: Procedure for Filing Pre-license/Pre-approval Inspection Material*.
3. For blood and blood components only
 - a. Notifies ORA of scheduled inspections and invites them to participate in the CBER-led inspection.
 - b. Prepares Endorsement based on the inspection documentation and the inspection close-out memo provided by BPB/DBA.
 - c. Returns inspection materials to BPB reviewer with the endorsement.

E. RPM: Inspectional Activities

1. If necessary, confirms with the DMPQ reviewer that pre-approval inspection teams have been identified and the inspection(s) initiated, in accordance with *SOPP 8410: Determining When Pre-License/Pre- Approval Inspections are Necessary*
2. Ensures completion of the inspection information in RMS-BLA and inclusion in the complete BLA final action package

VII. BLA: Final Action Activities

A. Review Committee: Approval Activities

1. Ensures that all appropriate documentation (review memos, telecons, etc) is entered in RMS-BLA and either imported into the EDR or forwarded to the RPM for inclusion in the final action package prior to routing the file for approval. All review memos should be signed by the reviewer and have the concurrence of the supervisor(s) before entry or routing.

B. Product Review Branch (PRB): Approval Activities

1. Ensures that all lots submitted in support of an application have been processed and any necessary testing has been satisfactorily completed. Documents this step on the Licensing Action Recommendation Memorandum (LARM) before approval
2. Obtains signoff from the Director, DMPQ/OCBQ on the Lot Release Testing Plan; forwards to QAS.

C. Division of Case Management (DCM)/OCBQ: Approval activities

1. Issues the compliance status check upon completion by sending via email or hard copy to the requestor per *SOPP 8407: Compliance Status Checks*

D. RPM: Approval Activities

1. Pre-Approval Notification:

- Notifies the Office of the Center Director and the Division of Communication and Consumer Affairs (DCCA), Office of Communication, Training and Manufacturer's Assistance (OCTMA) by including this information in OCTMA's weekly CBER summary report approximately **four weeks** prior to approval for a new indication or one for which there is significant public interest of the expected approval
2. Ensures that the compliance status check is acceptable. Notifies the committee chair if the compliance status check is unacceptable.

3. Ensures the compliance check request and response are entered into RMS-BLA and included in the final action package.
4. Verifies with PRB that lots are available for release at the time of approval and that the appropriate review and sign-off on the lot release protocols have been completed.
5. Ensures that the CBER Lot Release Testing Plan and Protocol Review Worksheet have been reviewed and signed off.
6. Prepares the Licensing Action Recommendation Memorandum (LARM).
 - a. The signoff routing for the LARM should include individuals listed on the form
7. Prepares the Approval Letter in accordance with *SOPP 8405: Complete Review and Issuance of Action Letters*.
 - a. Will bear the signature of the product Office Director and the OCBQ Office Director,
 1. If the applicant already has a license number, the approval letter will be signed by the product Office Director only. However, the letter will be routed through the Division Director, DMPQ
 2. Approval letters for blood and blood components are signed by the OBRR Office Director or designate only
 - b. The draft approval letter should be circulated electronically for a comment period 72 hours prior to final routing.
8. Ensures that pertinent secure emails are reflected in RMS-BLA and incorporated as part of the administrative record.
9. Ensures that a quality control check of the final action record file has been performed and all information is documented and entered into RMS-BLA before the 60 day RMS-BLA lockdown on data entry.
 - a. Once the RMS-BLA lockdown occurs, any documentation that needs to be added or deleted will need the authorization of the Associate Director for Review Management. The authorization request will go through the appropriate Division and Office Director.
10. Ensures that the status of the application is changed in RMS-BLA no later than 2 working days after approval
11. Sends the completed final action package to DCC for filing. Refer to *DCC Procedure Guide 8: Procedure for Filing Final Action Packages Containing FDA Correspondence for Marketable Applications* or *DCC Procedure Guide 9: Procedure for Filing Multiple Product Final Action Packages Containing FDA Correspondence for Marketable Applications*.
 - a. If applicable, the Summary of Basis for Approval (SBA) or cover memorandum from the SBA Equivalent reviews, and FONSI will be filed in the final action package behind the LARM
12. Ensures that the applicant is notified of the product approval (by telephone or facsimile) and the hard copy of the letter is sent
13. Ensures that copies of the dated approval letter or electronic notification are distributed to:
 - a. the Director of the appropriate product Office,
 - b. the Director of the Applications Division/Regulatory Management Staff,
 - c. members of the review committee and their respective Division Directors,
 - d. RIMS (HFM -110),
 - e. PRB (HFM – 672) so that lots may be released
 - f. DCCA/OCTMA ((HFM-43) include patient package insert if applicable)
 - g. Communication Technology Branch (CTB)/DCCA/OCTMA for web posting per *SOPP 8105: Submitting Documents for the CBER Web Sites*.
 - h. APLB/DCM/OCBQ (HFM-602) (include patient package insert if applicable)
 - i. Director, Division of Epidemiology (DE)/OBE (HFM-220) (include patient package insert if applicable)
 - j. QAS (HFM-4)
14. Ensures that when approving a new or expanded clinical indication a copy of the final draft

labeling, or final labeling if available, is sent to the Office of the Center Director and that a copy of the SBA (or Equivalent) is sent to DCCA/OCTMA per *SOPP 8106: Submission of Product Approval Information for Dissemination to the Public*

E. RPM: Withdrawal activities

1. Prepares the withdrawal acknowledgement letter to be sent to the applicant in accordance with *SOPP 8405: Complete Review and Issuance of Action Letters*.
 - a. The application withdrawal acknowledgement letter will bear the signature of the product Office Director or designate.
2. Ensures that a quality control check has been performed on all information documented and entered into RMS-BLA before the 60 day RMS-BLA lockdown on data entry.
 - a. Once the RMS-BLA lockdown occurs, any documentation that needs to be added or deleted will need the authorization of the Associate Director for Review Management. The authorization request will go through the appropriate Division and Office Director.
3. Ensures that the status of the application is changed in RMS-BLA no later than 2 working days after withdrawal
4. Sends the application, all appropriate CBER generated correspondence, and a copy of the signed withdrawal acknowledgement letter to DCC for filing. See *DCC Procedure Guide 8: Procedure for Filing Final Action Packages Containing FDA Correspondence for Marketable Applications* or *DCC Procedure Guide 9: Procedure for Filing Multiple Product Final Action Packages Containing FDA Correspondence for Marketable Applications*, as appropriate.
 - a. CBER generated documents that are signed electronically and imported into the EDR do not need to be printed and sent to DCC for filing.
5. Ensures the withdrawal acknowledgement letter is distributed to the product applications Division Director, the DMPQ Division Director, and QAS.

6. Effective Date

March 12, 2007

7. References

[Guidance for Industry Information Request and Discipline Review Letters Under the Prescription Drug User Fee Act](#)

[Guidance for Industry Providing Regulatory Submissions in Electronic Format – Biologics Marketing Applications \(BLA, PLA/ELA, and NDA\) November 1999 revised](#)

[SOPP 8001.4 Review of CBER Regulated Product Proprietary Names](#)

[SOPP 8101.1 Scheduling and Conduct of Regulatory Review Meetings with Sponsors and Applicants](#)

[SOPP 8104: Documentation of Telephone Contacts with Regulated Industry](#)

SOPP 8105: Submitting Documents for the CBER Web Sites (CBER's Intranet)

[SOPP 8106 Submission of Product Approval Information for Dissemination to the Public](#)

[SOPP 8114: Administrative Processing of Documents Received Prior to Submitting Investigational or Marketing Applications \(Pre-Application\)](#)

[SOPP 8401.1 Issuance and Review of Responses to Information Requests and Discipline Review Letters to Pending Applications](#)

[SOPP 8401.3 Filing Action: Communication Options](#)

[SOPP 8401.4 Review Responsibilities for the CMC Section of Biologic License Applications and Supplements](#)

[SOPP 8401.5 Processing of Animal Component Information Submitted in Investigational and Marketing Applications/Notifications](#)

[SOPP 8404 Refusal to File Procedure for Biologics License Applications](#)

[SOPP 8405: Complete Review and Issuance of Action Letters](#)

[SOPP 8406: Verification of User Fee Data Sheet and Payment](#)

[SOPP 8407 Compliance Status Checks](#)

[SOPP 8408: Collaboration of CBER Offices on Issues Related to the Release of Pre-Licensing and Routine Lots](#)

[SOPP 8410 Determining When Pre-License/Pre-Approval Inspections are Necessary](#)

[SOPP 8412 Review of Product Labeling](#)

[SOPP 8505 Nomination and Approval of CBER Inspectors and Product Specialist Assigned to Conduct Inspections of Biological Products](#)

Note: DCC Procedure Guides are located on CBER's Intranet

DCC Procedure Guide 8: Procedure for Filing Final Action Packages Containing FDA Correspondence for Marketable Applications

DCC Procedure Guide 9: Procedure for Filing Multiple Product Final Action Packages Containing FDA Correspondence for Marketable Applications

DCC Procedure Guide 11: Procedure for Filing Pre-License/Pre-Approval Inspection Material

DCC Procedure Guide 22: Procedure for Processing, Routing, and Storing Electronic Submissions

8. History

Written/Revised	Approved	Approval Date	Version Number	Comment
Linda Dixon	Robert A. Yetter, PhD	April 30, 2007	6	Revised to include information on PTS.
RMCC	Robert A. Yetter, PhD	March 9, 2007	5	Incorporates changes to describe lot release activities associated with product review and to include additional review activities
RMCC	Robert A. Yetter, PhD	May 11, 2003	4	Changes incorporating new SOPP 8104.3: Filing Action: Communications Options
RMCC	Robert A. Yetter, PhD	October 2, 2002	3	Changes accommodating PDUFA III and other updates

RMCC	Robert A. Yetter, PhD	February 22, 2000	2	Incorporates changes necessitated by publication of BLA final rule (64 FR 56441) and Biostatistics & Epidemiology change from Division to Office
		September 10, 1997	1	Original

Updated: May 1, 2007