SOPP 8401: Administrative Processing of Original Biologics License Applications (BLA) and New Drug Applications (NDA)

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I. Purpose

This Standard Operating Policy and Procedure (SOPP) serves as a guide to the Center for Biologics Evaluation and Research (CBER) staff for the administrative processing of Biologics License Applications (BLAs) and New Drug Applications (NDAs).

II. Scope

A. This SOPP applies to original BLAs and NDAs processed by CBER including those subject to the Biosimilar User Fee Act (BsUFA) and the Prescription Drug User Fee Act (PDUFA).

B. This procedure does not apply to:

1. BLAs subject to the Medical Device User Fee Act (MDUFA)
2. Abbreviated New Drug Applications (ANDAs) subject to the Generic Drug User Fee Act (GDUFA)
3. Annual Reports

III. Background

A. The BLA is a request for permission to introduce, or deliver for introduction, a biologic product into interstate commerce. A BLA is submitted by an applicant (manufacturer) and must contain data derived from non-clinical laboratory and clinical studies which, demonstrate that the manufactured product meets prescribed requirements of safety, purity, and potency (21 CFR Part 601.2).

B. The NDA is the vehicle through which applicants formally propose that a new drug be approved for sale and marketing in the United States (Federal Food, Drug, and Cosmetic Act (FDCA) section 505(b)).

C. The Patient Protection and Affordable Care Act amended the Public Health Service (PHS) Act to create an abbreviated licensure pathway for biological products that are demonstrated to be “biosimilar” to or “interchangeable” with an FDA-licensed biological product. The Biosimilar User Fee Act (BsUFA) authorized the FDA to assess and collect fees for biosimilar products.

D. The Prescription Drug User Fee Act (PDUFA) authorized the FDA to collect user fees from manufacturers of certain human drug and biological products.

1. PDUFA V established a review model, known as “the Program,” for original BLAs and new molecular entity (NME) NDAs. The goal of “the Program” is to improve the efficiency and effectiveness of the first cycle review process and, through improved communication and greater transparency, decreasing the number of review cycles necessary for approval.

2. Products subject to PDUFA user fees include most human drugs and biological drug products. Products exempted from PDUFA include the following:

   a. Whole blood or a blood component for transfusion.

   b. Bovine blood product for topical application licensed before September 1, 1992.

   c. Allergenic extracts licensed before October 1, 2022, and standardized allergenic extract products submitted in accordance with 21 CFR 680.3(e) pursuant to a notification to the applicant from CBER’s Director regarding

the existence of a potency test that measures the allergenic activity of an allergenic extract product licensed by the applicant before October 1, 2022.

d. Cord blood and peripheral blood stem cells separated from whole blood by physical or mechanical means for transfusion.

e. An in vitro diagnostic biologic product licensed under section 351 of the PHS Act. (These BLAs are subject to MDUFA.)

f. A biological product licensed for further manufacturing use only.

3. PDUFA VII established new milestones for CBER to meet the targeted communication date for any proposed postmarketing requirement (PMR) (Title IX, PREA, Accelerated Approval, or Animal Rule) as specified in the filing letter:

a. For standard new molecular entity (NME) NDAs and original BLAs, CBER will communicate details on anticipated PMRs no later than 8 weeks before the PDUFA action goal date.

b. For priority NME NDAs and original BLAs, CBER will communicate details on anticipated PMRs no later than 6 weeks before the PDUFA action goal date.

E. CBER developed the Managed Review Process (MRP) with the goal of providing a process to most effectively and efficiently review all user fee and non-user fee license applications and supplements. This process begins during the investigational phase which builds the foundation of information necessary to demonstrate safety, efficacy, and capability of consistent manufacture of a drug or biological drug product and continues through the postmarketing phase.

1. The MRP incorporates the fundamental values and operational principles contained in the draft *Guidance for Industry and Review Staff: Good Review Management Principles and Practices for New Drug Applications and Biologics License Applications*.

2. CBER's MRP consists of all CBER regulatory SOPPs, checklists, job aids, references, and templates, including letter and review templates that help CBER's review community carry out their review responsibilities.

F. Complementary to the MRP during the review and decision-making process are advisory committees (ACs). They provide independent advice and recommendations to the FDA on scientific and technical matters related to the development and evaluation of products regulated by the Agency. The FDA requests advice from ACs on a variety of matters, including various aspects of

clinical investigations and applications for marketing approval of drug products. Advisory committee members are scientific experts such as physician-researchers and statisticians, as well as representatives of the public, including patients. Although the ACs provide recommendations to the Agency, final decisions are made by the FDA.

IV. Definitions

A. Amendment – Information submitted to a pending submission, including additional information or reanalysis of data previously submitted to clarify, revise or modify the application as originally submitted.

1. **Major Amendment –** An amendment to an original application, efficacy supplement, manufacturing supplement or resubmission of any of these applications, including biosimilars, that extends the review clock.

2. **Unsolicited Amendment –** A submission of information or data from the applicant that the Agency has not requested.

B. Complete Response (CR) Letter – A letter issued when the complete review indicates that there are deficiencies remaining that preclude the approval of the application at that time. **Note**: A CR letter stops the review clock. The CR letter will summarize all the remaining deficiencies and describe actions necessary to place the application in a condition for approval.

C. Deficiencies Identified (Day 74) Letter – A letter notifying the applicant of issues identified during the filing review phase that were not communicated in the filing letter.

D. Establishment inspection report (EIR) – The report issued at the conclusion of an establishment inspection that summarizes the inspectional findings.

E. Expedited Review – FDA's review of a human drug application that has received priority review designation where the Review Team (Committee) plans to act at least 1 month before the PDUFA goal date provided that no significant application deficiencies prevent an early action.

F. Filing Letter – A letter issued to notify the applicant that their submission has been filed and will be reviewed. **Note:** The filing letter also includes information stipulated by PDUFA and may contain any identified filing deficiencies.

G. Information Request (IR) Communication – A communication sent to an applicant during submission review to request further information or clarification that is needed to complete review.

H. **Late-Cycle Meeting (LCM) –** A meeting held for applications subject to the PDUFA Program with the CBER Review Committee, CBER senior management, and the applicant to discuss the status of the review of the application late in the review cycle. **Note:** This meeting is not intended to discuss the pending regulatory decision on the application.

I. **Letter Ready Comments –** Written comments formulated by the reviewer(s) of a submission written sufficiently well (e.g., correct grammar, spelling, punctuation) to be readily included in a communication (not always a letter) to the applicant.

J. **Mid-Cycle Communication –** A phone call to the applicant that generally happens within two weeks following the internal Mid-Cycle review meeting to provide the applicant with an update on the status of the review of their submission. **Note:** This applies to submissions subject to the PDUFA/BsUFA Programs only.

K. **Primary Discipline Review –** A written review containing a reviewer's assessment and recommendations of all assigned areas of the original submission.

L. **Priority Review –** A reduced review schedule compared to a standard review schedule to potentially allow the product to reach the market faster.

M. **Regulatory Communication –**A communication that contains regulatory information, including correspondence generated by CBER. The inclusion of a submission's submission tracking number (STN) makes a communication regulatory in nature.

N. **Review Memorandum Addendum –** Information appended to a previously finalized review memorandum. **Note:** This addendum may include a written review of any amendments that have been accepted for review by CBER since the primary discipline review was completed and documented, any AC recommendations, and/or results or actions stemming from issuance of an establishment inspection report (EIR).

O. **Secondary Discipline Review –** A review by the Division Director and by intervening supervisory (i.e., Branch or Laboratory Chief) or non-supervisory (Team Lead) reviewers of the primary discipline review memo.

P. **Standard Review –** All non-priority applications are considered standard applications.

Q. **Substantive Review Issues –** Issues identified to date that may preclude approval if not resolved.

R. Summary Basis of Regulatory Action (SBRA) – A summary of all relevant and pertinent information from the review of a BLA or NDA. **Note:** The SBRA documents conclusions from all review disciplines (clinical, statistical, CMC, pharmacology/toxicology, etc.) about the product, notes any critical issues and disagreements with the applicant and within the FDA Review Committee and how they were resolved, provides recommendations for action and an explanation of any non-concurrence with review conclusions, and provides a detailed discussion of areas in which there were notable issues, unusual aspects or problems with the data or analysis, novel features of design, or conduct of studies.

S. Universal Review Memo Smart Fill Template - A smart fill template with a standardized framework to structure documentation of CBER submission reviews, ensuring consistency in meeting regulatory and quality elements.

V. Policy

A. All new marketing applications for products subject to licensure under the PHS Act are handled as BLAs. The procedures in this SOPP are not inclusive of all detailed procedures used to process applications. This SOPP is to be used with other related SOPPs, such as *SOPP 8412: Review of Product Labeling* and others listed in the references section, that describe administrative handling and review of license applications. NDAs are managed in the same manner as BLAs where appropriate. Differences in NDA handling are described in the Procedures section of this SOPP as needed.

B. Requirements for electronic submissions:

1. Under Section 745A(a) of the Federal Food, Drug, and Cosmetic Act (FDCA), applicants are required to submit information electronically in the appropriate FDA-supported formats (electronic common technical document (eCTD)) for certain BLAs, NDAs, ANDAs and supplements to these submission types with the exception of devices and blood and blood components, including source plasma submissions.

2. Submissions that are required to be eCTD compliant but are not submitted electronically or electronic submissions that are not in a format that FDA can process, review, and archive, will not be filed or received, unless exempted from these requirements.

3. Submissions that are not required to be in eCTD format (e.g., submissions for blood and blood components) should be submitted as directed on the FDA's eSubmitter website (FDA eSubmitter).

4. Please see the *Guidance for Industry: Providing Regulatory Submissions in Electronic Format: Certain Human Pharmaceutical Product Applications and*

Related Submissions using the eCTD Specifications, under References, for complete eCTD requirements and exceptions.

C. Formal submissions (e.g., new INDs, original BLAs, etc.), information that is unsolicited, or that FDA did not agree to receive related to pending applications, are not to be transmitted via email. Any such emails will not be accepted or included in the administrative file. Please refer to CBER's *SOPP 8119: Use of Email for Regulatory Communications* for more information.

D. In order for FDA to send regulatory communications via email, the email must be sent to a secure email partner, to allow the FDA to digitally sign and encrypt the message. For further information regarding secure email, please refer to CBER's *SOPP 8119: Use of Email for Regulatory Communications*.

E. A signed Form FDA 356h should be submitted with all BLA/NDA-related applications and correspondences to CBER. This information will aid in routing the application to the appropriate division for processing. The person who signs an FDA application form (e.g., Form FDA 356h) is presumed to have signatory authority for the company and therefore should be considered an Authorized Official of the company when submitting a BLA. Accordingly, the signatory of the original application, or designee, should sign all amendments submitted to CBER.

F. If an application orientation meeting (AOM) is requested, CBER will make every effort to grant the applicant's request based on the availability of resources.

G. Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov (Form FDA 3674) should be included with all applicable submissions, i.e., originals and amendments. The applicant is to determine the relevance of the application for compliance with Title VIII of the Food and Drug Administration Amendments Act (FDAAA) and check the appropriate box on the form. The applicant should also indicate on the form the National Clinical Trial (NCT) number(s) that apply.

H. If an application is not filed by CBER (refer to *SOPP 8404: Refusal to File Procedures*), and the applicant does not request that the application be filed over protest or follow the procedures for filing over protest [refer to *SOPP 8404.1: Procedures for Filing an Application When the Applicant Protests a Refusal to File Action (File over Protest)*], no additional submissions can be made to that application. The applicant must submit a new application, along with any applicable user fees.

I. Applications filed over protest after a refuse to file decision are not eligible for parameters of the PDUFA Program. The original submission will be subject to the review goals per the current PDUFA goals letter; resubmission goals do not apply. Refer to *SOPP 8404.1: Procedures for Filing an Application when the*

Applicant Protests a Refusal to File Action (File Over Protest) for additional information.

J. For products covered by user fees, the performance goals established in the most current user fee goals letter will be met.

K. Applications for non-user fee products will not be subject to all the procedures of the PDUFA/BsUFA Programs but will be subject to CBER's Managed Review Process. Differences in handling submissions not subject to the PDUFA/BsUFA Programs are described in the Procedures section as needed.

L. Review assessment and its documentation starts when the application is received and progresses throughout the review timeline, such that the primary discipline review must be nearly complete, if not complete, by the target date in time for the Mid-Cycle meeting.

M. Where available, CBER reviewers will use reviewer templates that have been developed and approved specifically for their assigned areas of responsibility. The use of reviewer templates promotes consistency in the documentation of elements and enhances comprehensive reviews.

N. Where a reviewer template is not available, CBER reviewers will use the Universal Review Memo Smart Fill Template. The use of the universal review memo supports consistency in the documentation of elements and enhances comprehensive reviews.

O. Under normal circumstances, product lot(s) should be available for distribution at the time of approval of most BLAs. Exceptions will be made on a case-by-case basis. Please refer to *SOPP 8408.1: Development of Laboratory Quality Product Testing Plans and Release of Lots as Part of the BLA Approval Process* for additional information.

P. CBER staff will not discuss the pending regulatory status for a submission with the applicant while the submission is still under review. The regulatory action may only be discussed after the final decision is conveyed to the applicant.

Q. The original application submission is expected to be complete per 21 CFR 601.2 and 21 CFR 314 (unless rolling review has been agreed upon).

1. For products subject to the PDUFA/BsUFA Programs, the CBER Review Committee Members and the applicant may agree at the pre-submission meeting on minor application components that are allowed to be submitted not later than 30 calendar days after receipt of the original submission of the application.

2. For products subject to the PDUFA/BsUFA Programs, the only components allowed to be submitted more than 30 calendar days after the original application include stability and clinical safety updates. The dates when these are to be provided should be discussed at the pre-submission meeting.

3. Incomplete submission of an application, including failure to provide agreed upon information within 30 days of receipt of the application, will be subject to a refuse to file decision. Please refer to *SOPP 8404: Refusal to File Procedures* for additional information.

R. Marketing applications for fast track, breakthrough therapy, and/or regenerative advanced medicine therapy (RMAT) designated products may be eligible for priority review, accelerated approval, and/or rolling review as described in the *Guidance for Industry: Expedited Programs for Serious Conditions - Drugs and Biologics*. Ideally, if a rolling review has been granted, all portions of the application should be submitted no more than one year after the initial portion. Any review of portions already submitted may be suspended because our ability to conduct a meaningful review may be inhibited without the missing information.

S. Review Timeline:

1. For products subject to the PDUFA/BsUFA Programs, the review timeline begins upon the acceptance of the original application submission for filing, no later than 60 calendar days from the date that CBER receives the application.

2. For products subject to PDUFA but not subject to the PDUFA Program, the review timeline begins upon CBER receipt of the application.

3. For non-user fee applications, the review timeline begins upon CBER receipt of the application.

4. For products subject to PDUFA, each application will be evaluated on a case-by-case basis to determine if the review timeline will be an expedited, priority, or standard review timeline.

a. Products are eligible for priority review if they provide a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious or life-threatening disease.

b. The review and administrative processing for expedited review submissions will follow the same procedures for all BLAs/NDAs but require condensed timelines to ensure action occurs at least one month before the goal date.

c. If the Review Committee determines, after the applicant is notified in the Filing Letter, that an expedited review is no longer appropriate, the timeline will default to priority. The decision for the change in review timelines should be communicated to the applicant within 3 business days of making the decision.

i. If there is an upcoming meeting with the applicant, the decision should be discussed during the meeting and included as part of the meeting summary.

ii. If the applicant is notified via telecon, the telecon summary will be sent to the applicant.

iii. Reasons an expedited review may no longer be appropriate:

a) Unexpected application deficiencies are found,

b) The marketing application is of poor quality,

c) The applicant fails to engage in collaborative communications (e.g., failure to respond in a timely manner to Information Requests (IRs),

d) Unanticipated review issues arise, or

e) Facilities are not ready for inspection.

5. Timeline extensions for products subject to the PDUFA/BsUFA Programs:

a. If, during the FDA's review of an original application, the Agency identifies a manufacturing facility that needs to be inspected and was not included in the comprehensive and readily located list, the goal date may be extended by 3 months.

b. The submission of a Major Amendment at any time during the review cycle may extend the goal date by 3 months.

c. Note: there may be only one extension during the review cycle.

T. Filing:

1. Filing meetings are expected to occur. However, filing meetings for non-user fee products occur as needed when the application is incomplete or when other issues are identified by the Review Committee Members.

2. Before the Filing meeting each reviewer is expected to document in the appropriate discipline specific Filing Review Checklist or a review memorandum any potential issues with the application that could result in a

refuse to file decision or be included in the Deficiencies Identified (Day 74) letter.

3. Generally, if deficiencies have been identified during the filing review that are not refuse to file issues they will be communicated in the filing letter at day 60.

T. Unsolicited amendments are discouraged; however, in some cases (e.g., new adverse reaction, safety information, manufacturing information, etc.) such amendments may be necessary.

U. Unsolicited amendments, including responses to issues identified in the filing letter and responses to a Day 74 letter, will be reviewed in accordance with the underlying principle that the most efficient path toward completion of a comprehensive review that addresses deficiencies and leads toward a first cycle approval when possible, will be considered and as resources permit. However, CBER will not usually review an unsolicited amendment after the review of the application is complete and the issuance of an action letter is imminent (i.e., the type of action letter has been decided, and comments are being drafted).

V. Mid-Cycle Meeting:

1. By the Mid-Cycle Meeting, each reviewer is expected to document their review progress in their assigned areas of responsibility in a primary discipline review memorandum that summarizes content, documents the reviewer's assessment, and identifies key issues identified to date.

2. At the Mid-Cycle Meeting, each reviewer is expected to discuss key findings documented in the primary discipline review memorandum. A Reviewer Report that summarizes substantive issues copied from the primary review memorandum and a proposed plan to address these issues must be provided by email to the Regulatory Project Manager (RPM) in advance of the meeting.

3. For non-user fee products, formal Mid-Cycle Meetings are encouraged and will be conducted on an as-needed basis.

4. For products subject to the PDUFA/BsUFA Programs, the RPM and the Review Committee Chair will have a Mid-Cycle Communication telecon with the applicant within two weeks following the Mid-Cycle Meeting to provide an update on the status of the review. Review Committee Members may attend as appropriate for discussion of issues regarding their review discipline. If there are no issues to discuss, then the Mid-Cycle Communication telecon may be cancelled at the request of the applicant.

W. Late-Cycle Meeting (LCM) for submissions that qualify under the PDUFA/BsUFA Programs:

1. The purpose of the Late-Cycle Meeting is to:

a. Discuss the progress of the review,
b. Identify and present substantive issues and plans to address those issues,
c. Discuss the remainder of the review including possible dates for further deliverables and interactions.

2. CBER staff will not discuss the pending final regulatory action with the applicant.

3. The Office Director and/or Deputy Office Director, Review Committee Members, and Team Leaders or Supervisors from disciplines with substantive issues must be present at the LCM. The meeting must be rescheduled if the Office Director or Deputy Office Director cannot attend.

4. LCM generally will be granted in the format requested.

5. The LCM materials will be sent to the applicant no later than 10 calendar days (or 2 calendar days for an expedited review) before the LCM.

6. If there are no issues to discuss, the Late Cycle meeting may be cancelled at the request of the applicant.

X. Advisory Committee (AC) Meetings (if applicable):

1. For PDUFA products: Should occur no later than 2 months (standard review) or no later than 6 weeks (priority review) before the user fee goal date.

2. For BsUFA products: Should occur no later than 3 months before the user fee goal date.

3. The Designated Federal Officer (DFO) will send the Agency briefing materials to the applicant based on the timelines in the *Guidance for Industry Advisory Committee Meetings – Preparation and Public Availability of Information Given to Advisory Committee Members*.

4. The DFO will provide final questions for the AC meeting to the applicant and the AC members at least 2 business days before the AC meeting.

5. If the AC meeting is scheduled earlier than when the Late-Cycle Meeting occurs (due to AC scheduling outside the Review Committee's control), only the briefing materials for the AC meeting will be sent to the applicant.

Y. It is critical that the Review Committee Members keep management, including Office and Center senior management, up to date with any significant review issues. Additionally, all communications, including telephone calls and other informal communications are to be continuously entered into all appropriate regulatory systems in real time; all documents should be uploaded through CBER Connect into the administrative file. All letters issued by CBER must use the most recently approved template found in CBER's Letter Templates Library.

Z. Defined dates used on CBER correspondence and entered into CBER systems are described in regulatory job aid JA 820.02: Dating of CBER Regulatory Correspondence. CBER correspondence includes letters, internal memoranda, meeting or telecon minutes, and internal or outgoing emails or facsimiles (fax).

AA. An internal post action meeting may be held with all members of the Review Committee within 45 days of ending the first review cycle (i.e., issuing the first CR or approval) to discuss the Review Committee dynamics, interactions with the applicant, basis of decisions, what worked well, and what didn't work well during the review cycle. The goal is to identify improvements that can be made within Review Committee dynamics and Center or Office procedures. A summary of the meeting, including specific recommended changes, should be recorded and communicated to the Associate Director for Review Management (ADRM), who will disseminate as appropriate to other CBER staff.

BB. All CBER correspondence should be correctly characterized and entered in the appropriate regulatory system and uploaded into the administrative file before the final action (e.g., approval, withdrawn, refuse to file). After the final action is taken, applicant amendments will be allowed to the submission for 14 calendar days. Changes to CBER communications/documents will be allowed for 30 calendar days. After these timeframes, a lockdown will be initiated, and no additional or revised documents will be added to the submission without approval. Refer to Regulatory *Job Aid 910.08: Lockdown of Applicant Submissions and CBER Correspondence for Marketing Submissions* for additional information.

CC. In limited circumstances, an applicant may submit two BLAs/NDAs for the same product that are concurrently reviewed as stand-alone applications with separate STNs. This occurs when an applicant has a pending BLA/NDA and seeks approval for another reason (for example a different indication or dosage) for the same product (refer to the Guidance for Industry: Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees). The first application approved will be designated as the "parent" and the second

application approved will be designated as the “child.” After approval of the child application, it will be administratively closed and consolidated with the parent STN. No subsequent submissions to the child STN will be accepted. For more information, CBER reviewers should refer to SOPP 8401.8: Procedures for Consolidating Two STNs (original applications of BLAs/NDAs) for the Same Product from the Same Applicant.

1. To consolidate the two applications into one STN,

a. After the parent application is approved, and while the child application is still under review,

i. An amendment should be submitted to the child STN that includes the parent approved labeling and a letter of cross-reference to the parent STN to ensure that the labeling (e.g., package insert) is consistent.

AND

ii. A labeling prior approval supplement (PAS) must be submitted to the parent STN to incorporate the indications/changes in the child application. This should happen while the child STN is still under review to allow concurrent review and approval of both STNs to allow consolidation into a single STN (i.e., the parent STN) at the time of the approval of both submissions.

b. In rare cases, there may be circumstances where concurrent review of the child application and the labeling PAS to the parent is not feasible. It is advisable for applicants to contact the appropriate review office for instructions in the event concurrent review is not possible.

c. Any changes made to the parent STN, but not incorporated yet into the child STN should also be submitted to the child STN by an amendment.

2. A request for the review of the same proprietary name should only be submitted to the parent STN.

3. The lot release protocol should be established under the parent STN.

4. Any postmarketing requirements/commitments (PMR/PMCs) that are required for the child STN will be listed only in the approval letter for the parent labeling PAS, not in the approval letter for the child. The numbering for the PMR/PMC for the child will begin where the parent numbering ends, e.g., if there are 5 PMCs for the parent, the number for the first child PMC will begin at 6.

VI. Responsibilities

A. **Review Committee Chair (Chair) –** Discusses and assures resolution of scientific issues and associated regulatory interpretations in concert with management. Specific responsibilities include ensuring that all sections of the application have been assigned for review, drafting of the SBRA, bringing scientific issues to the attention of management, and facilitating resolution and consensus. The Chair works closely with the RPM in executing these duties. (Note: The cross-discipline team leader (CDTL) as referred to in the PDUFA Program is considered the chair within CBER.)

B. **Office Director, Deputy Office Director –** The Signatory Authority who signs first action letters (e.g., those that stop the review clock such as a complete response, approval, or refuse to file).

C. **Division Director** - The signatory authority who signs regulatory letters, as appropriate, and concurs or does not concur with the reviewer's assessments and recommendations.

D. **Regulatory Project Manager (RPM) –** Responsible for the overall management of the review. Specific responsibilities include scheduling Review Committee Meetings, ensuring regulatory and administrative actions are completed on time, notifying management when timelines are not met, reviewing assigned sections, performing quality control checks, capturing Review Committee communications, ensuring regulatory systems are updated, and ensuring the file is administratively complete.

E. **Review Committee Members –** Each member performs a review of all assigned areas of submissions, participates in Review Committee Meetings, and documents the review by completing the appropriate documentation, including but not limited to, the appropriate Filing Review Checklist and a Discipline Review Memo; correctly characterizes and enters all appropriate documentation into the appropriate regulatory system and uploads them into the administrative file. This review should be scientifically sound and follow Good Review Management Principles and Practices.

F. **Supervisors –** Ensures that the overall content of reviews are appropriate, all administrative processing steps are completed, including data entry, and all deadlines are met. Reviews and approves employee's review documents and other submission documents per CBER policies and procedures.

VII. Procedures

A. General Information

1. Each step in the procedure section is chronologically listed where practicable. It is permissible to accomplish steps out of sequence when appropriate. Some steps in the process will not apply to non-user fee products.

2. Refer to *C 910.04: PDUFA Checklist for Original BLAs and Supplements* for additional information related to review timelines.

3. Refer to *R 910.05: Formal Communication Plan for Interactions and Information Exchange between the Applicant and FDA during Review of an Original BLA or NME NDA* for additional information on a Formal Communication Plan.

B. Receipt of Application

1. Electronically receive, process, validate, and load into CBER Connect. Notify the appropriate Office of submission accessibility through the CBER Connect load notification. **[Electronic Submission Program Manager (ESPM)] Note:** CBER Connect will route the application based on the product name as reported by the applicant on the Form FDA 356h following current routing workflows.

2. Determine if the user fee is paid and notify the PDUFA User Fee Staff to perform user fee verification: **[RPM]**
   a. Refer to *SOPP 8406: CBER Processing of PDUFA Application Payments*
   b. Refer to *Guidance for Industry: Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees* for additional information.

3. Ensure that the information on the PDUFA User Fee Cover Sheet (Form FDA 3397) is accurate. Enter the User Fee Identification Number and payment date into the appropriate regulatory system for products subject to user fees. **[PDUFA User Fee Staff]**

4. Notify the RPM if user fee payment has not been received. **[PDUFA User Fee Staff]**

   a. If user fee payment is not received within five calendar days of the CBER receipt date:
      i. Notify the applicant using the CBER Acknowledgement Letter template; make certain to include the “unacceptable for filing” paragraph. Refer to CBER’s Review Letter Templates in CBER’s SharePoint Online (SPO) library for the most recently approved template. **[RPM]**

      ii. Inform the Review Committee Members to halt review. **[RPM]**

      iii. Ensure the letter is correctly characterized, entered into the regulatory system, and uploaded into the administrative file. **[RPM]**

5. Ensure that Form FDA 3674 (for clinical trials) was submitted, that all information necessary was provided, and the information is included in the appropriate regulatory system. **[RPM]**

    a. If the form was not submitted, contact the applicant to request it, document request in the appropriate regulatory system and upload it into the administrative file.

6. Ensure a Submission Tracking Number (STN) is assigned. **[RPM]**

7. Identify and enter all data, including the short summary and characteristic codes (e.g., breakthrough therapy, fast track, or RMAT designation, rolling review, combination product type, reference product exclusivity request, orphan product exclusivity, orphan drug designation, rare pediatric disease designation, priority review voucher, accelerated approval requests) and ensure all necessary fields are completed in the appropriate regulatory system. **[RPM]**

8. Identify other submissions: **[RPM]**

    a. Identify any submissions referred to by the applicant (Form FDA 356h and within application).

    b. Enter these referenced submission numbers in the appropriate regulatory system.

    c. Check the pre-marketing regulatory systems for any related investigational submissions and ensure cross-references are listed in the appropriate regulatory system. If appropriate, close any pre-marketing submissions, refer to *SOPP 8114: Administrative Processing of Documents Received Prior to Submitting Investigational or Marketing Submissions (Pre-Applications)* for additional procedures.

    d. Request a copy of any referenced Drug Master Files to be routed to appropriate reviewers as necessary.

9. Check daily for incoming submissions containing standardized study data and, if present, follow *SOPP 8401.12: Study Data Validation Process* to request that a CDISC format validation be performed. **[CBER Data Standards Representative]**

    a. After the validation report is available, schedule a study data meeting to discuss the data, including the validation with the review team. Meeting attendees should include the Data Standards Representatives, review team members responsible for reviewing studies with standardized study data (e.g., clinical, statistical,

pharm/tox), the Clinical Data Analyst if one is assigned, and the RPM. **[RPM]**

b. If revisions/corrections are needed after the validation report is presented to reviewers, send an Information Request (IR) to the applicant, correctly characterize, enter it into the regulatory system and upload it into the administrative file. **[RPM]**

c. Check to ensure that the "CDISC" STN Characteristic has been entered into the Submission Information screen. **[RPM]**

10. Determine if the Pediatric Research Equity Act (PREA) is triggered and notify the office Pediatric Review Committee (PeRC) representative if appropriate. **[RPM]**
Note: PREA is triggered when an application for a drug or a biological product is submitted for:

a. a new indication,
b. new dosing regimen (any change in a single dose, maximum daily dose or dosing interval),
c. new active ingredient (including a new combination),
d. new dosage form (e.g., vial to transdermal patch), or
e. a new route of administration (e.g., subcutaneous to intramuscular).

11. Notify the appropriate supervisors of receipt of the application requesting assignment or confirmation of Review Committee Members, including the following as applicable: **[RPM]**

a. Chair
b. Clinical Reviewer [product office]
c. Clinical Pharmacology Reviewer [product office]
d. Toxicology Reviewer [product office]
e. Developmental Toxicology Reviewer [product office]
f. CMC Reviewer [product office]
g. Office of Compliance and Biologics Quality (OCBQ)
  i. DMPQ Reviewer
  ii. DMPQ/PRB
  iii. APLB Reviewer
  iv. BIMO Representative
  v. DBSQC or OVRR/LIB Representative, as appropriate
  vi. DMPQ RPM
  vii. DMPQ Lead Inspector
h. Office of Biostatistics and Pharmacovigilance (OBPV)
  i. DB Statistical Reviewer of clinical data
  ii. DB Statistical Reviewer of Non-Clinical Data
  iii. Clinical Data Analyst

iv. DPV Postmarketing Safety Pharmacovigilance Reviewer
v. Digital Health Technology (DHT) Reviewer
vi. Real World Evidence (RWE) Reviewer
vii. Benefit-Risk Assessment Reviewer
viii. Artificial Intelligence (AI) Reviewer

i. Animal Pharmacology Reviewer
j. CMC Inspector
k. Labeling
l. Consult Reviewer (another Center). Refer to *SOPP 8001.5: Inter-Center Consultative Review Process* for more information.

12. Assign Review Committee Members and notify RPM. **[Supervisor/Triage Groups]**

13. Ensure that all Review Committee Members have been entered into the appropriate regulatory system. Follow-up with offices, if necessary, if assignments have not been made. **[RPM]**

14. Send the name(s) of the product reviewer(s) assigned to review the animal, biological, chemical component/information, if applicable, to the DCC Data Abstraction Team (DAT). **[RPM]**

a. Refer to *SOPP 8401.5: Processing Animal, Biological, Chemical Component Information Submitted in Marketing Applications and Supplements* for additional information.

15. Initiate review, including the need to conduct pre-approval/pre-licensure facility inspections, and determine if the application can be filed. See Filing section below for details. **[Review Committee Members]**

a. Ensure that all files can properly open, including PDFs and study data files. If problems are noted, contact the RPM.

b. Determine if cross-referenced Master Files are needed to provide a complete review. If needed, contact the RPM.

c. If the discipline Filing Review Checklist or memo will contain multiple reviews, designate the discipline reviewer responsible for uploading the checklist into the administrative file, as appropriate. **Note:** Each discipline reviewer may upload a separate Filing Review Checklist.

16. Determine if the product meets the definition of a combination product as defined in 21 CFR 3.2(e). If the product is a combination product, ensure the correct identification and categorization of the combination product on Form FDA 356h, and in the appropriate regulatory system, refer to *R 810.11:*

Combination Product Characterization Codes for more information. **[Review Committee Members, RPM]**

17. Issue an STN Acknowledgment letter to the applicant, correctly characterize and enter it into the regulatory system, and upload it into the administrative file through CBER Connect. **[RPM]**

18. Establish/confirm a draft review schedule, including the following, as applicable: **[RPM, Chair]**

    a. First Committee Meeting
    b. Filing Meeting
    c. RTF Briefing
    d. Internal Mid-Cycle Meeting
    e. Mid-Cycle Communication Telecon (with the applicant)
    f. Labeling Meetings
    g. Internal Late-Cycle Meeting
    h. Late-Cycle Meeting (with the applicant)
    i. PeRC meeting
    j. Other meetings as necessary (i.e., advisory committee, CBER Safety Working Group (SWG) if there are postmarketing requirements)

19. Schedule all review meetings using Microsoft Outlook, inviting all Review Committee Members, supervisors, and senior management as appropriate. **[RPM]**

    a. Refer to *R 910.02: Attendee Table for BLA/NDA Meetings* to determine required attendees.

C. First Committee Meeting

1. Draft and distribute the agenda for the First Committee Meeting (if not already provided in the formal meeting invite) no later than two days prior to the meeting using the *T 910.15: First Committee Meeting Agenda/Summary* template. **[RPM]**

2. Conduct First Committee Meeting. **[Chair, RPM]**

3. Ensure that decisions regarding the need for pre-license or pre-approval facility inspections (refer to *SOPP 8410: Determining When Pre-License/Pre-Approval Inspections are Necessary*) and/or Bioresearch Monitoring (BIMO) clinical site inspections are made as soon as possible. **[Review Committee Members]**

   Note: If a BLA Pre-License or NDA Pre-Approval inspection is deemed necessary, FDA's goal is to communicate its intent to inspect a manufacturing facility at least 60 days in advance of the inspection and no

later than mid-cycle. However, in accordance with the PDUFA VII commitment letter, FDA reserves the right to conduct manufacturing facility inspections at any time during the review cycle, whether or not FDA has communicated to the facility the intent to inspect.

4. Draft First Committee Meeting summary and identify follow-up activities. Circulate it to the Review Committee Members for comment. **[RPM]**

5. Review and comment or concur on the First Committee Meeting summary. **[Review Committee Members]**

6. Collate revisions for the First Committee Meeting summary and send it to the Chair for signature. **[RPM]**

7. Sign the First Committee Meeting summary and send it to the RPM. **[Chair]**.

8. Finalize First Committee Meeting summary, correctly characterize, enter it into the appropriate regulatory system, and upload it into the administrative file through CBER Connect. **[RPM]**

D. Filing Decision

1. Perform review in preparation for the Filing Meeting using the appropriate discipline specific Filing Review Checklist (e.g., CMC, Clinical). If there is no specific Filing Review Checklist, submit review in a Filing Review Memo or use the Universal Review Memo Smart Fill Template. **[Review Committee Members]**

   a. Refer to *JA 910.06: Completing a Filing Review* for additional information.

   b. Ensure that the application contains the information and data agreed to during the pre-BLA/NDA meeting, except for applications under the PDUFA/BsUFA Programs.

      i. Applications under the PDUFA Program are allowed to submit stability and clinical safety updates not later than 30 calendar days after receipt of the original application.

      ii. Applications under the BsUFA Program are allowed to submit stability and clinical safety updates or a limited amount of data from an assessment of a single transition from the reference product to the proposed biosimilar biological product, where applicable, no later than 30 calendar days after receipt of the original application.

2. Complete the appropriate Filing Review Checklist or Filing Review Memo before the Filing Meeting. **[Review Committee Members]**

Note: CMC Filing Checklist should be completed by the DMPQ Reviewer, the product reviewer, and the DBSQC Representative.

a. Notify the Chair, RPM, and supervisors (Branch/Lab Chief, Division Director) of a potential Refuse to File (RTF) recommendation. **[Review Committee Members]**

i. Alert the supervisory chain immediately upon discovering that a RTF recommendation may be made. **[Chair]**

ii. Follow *SOPP 8404: Refusal to File Procedures*.

3. Draft and distribute the Filing Meeting agenda in preparation for the Filing Meeting (if not already provided in the formal meeting invite) no later than five days before the meeting using the *T 910.16: Filing Meeting Agenda/Summary* template. **[RPM]**

4. Hold the Filing Meeting. At the Filing Meeting, each reviewer is expected to discuss the content of the application and present an overview of their relevant portion of the submission. **[Review Committee Members]**

a. Confirm the File or Refuse to File decision. **[Chair, RPM]**

i. File: Confirm the review schedule.

ii. Refuse to File: Document the RTF decision. Any recommendation for not filing the submission must include a list of missing, incomplete, or inaccessible information.

a) If RTF is recommended, ensure that the upper management briefing procedures are followed, refer *JA 910.22: Procedures for Upper Center Management Leadership Briefing Before Issuing a Refuse-to-File (RTF) Letter.*

5. Update the Filing Review Checklist or Filing Review Memo and obtain First Level Supervisor review and signature. **[Review Committee Members]**

6. Review and sign the Filing Review Checklist or Filing Review Memo; then forward it to Division Director. **[Supervisors]**

7. Review and sign the Filing Review Checklist or Filing Review Memo, then return it to Review Committee Member. **[Division Directors]**

8. Enter Filing Review Checklist or Filing Review Memo in the regulatory system, correctly characterize and upload it into the administrative file through CBER Connect. **Note**: Enter the name of the specific review discipline in the Summary Text. **[Review Committee Members]**

9. Draft the Filing Meeting Summary using the *T 910.16: Filing Meeting Agenda/Summary* template, and document the decision made at the Filing Meeting using information from the Filing Meeting agenda. Circulate to all Review Committee Members for review. **[RPM]**

10. Review and comment on the Filing Meeting Summary. **[Review Committee Members]**

11. Finalize the Filing Meeting Summary. **[RPM, Chair] Note:** The Chair is the signatory authority.

12. Sign the Filing Meeting Summary. **[Chair]**

13. Correctly characterize and enter the Filing Meeting Summary into the regulatory system and upload it into the administrative file through CBER Connect. **[RPM]**

14. Draft and circulate the Filing Letter upon concurrence of a filing decision. **[RPM] Note:** If deficiencies are included in the Filing Letter, circulate it to the Review Committee Members and supervisors for review.

15. Sign the Filing Letter; return it to RPM. **[Division Director]**

16. Issue the Filing Letter to the applicant; correctly characterize and enter the Filing Letter in the regulatory system and upload it into the administrative file through CBER Connect. **[RPM]**

17. Ask the applicant if lots for testing could be available should the Review Committee Members find a need to test the product in support of the application (for products subject to lot release). See *SOPP 8408.1: Development of Laboratory Quality Product Testing Plans and Release of Lots as Part of the BLA Approval Process*. **[Chair]**

18. Discuss with the applicant the need for an advisory committee (AC), if applicable. **[Chair, RPM]**

E. Deficiencies Identified (Day-74) Letter, if necessary

1. Document, in a review memorandum with supervisory concurrence, any potential issues that should be communicated to the applicant by Day-74 of the receipt of the application. **[Review Committee Members]**

2. Draft a Deficiencies Identified Letter that includes all issues identified in the Filing Meeting but not included in the Filing Letter; circulate it to the Review

Committee Members. Refer to CBER's Review Letter Templates in CBER's Letter Template SPO library for the most recently approved template. **[RPM]**

3. Review and comment or concur on the Deficiencies Identified Letter. **[Review Committee Members]**

4. Finalize the Deficiencies Identified Letter and send it to Division Director for signature. **[RPM]**

5. Sign the Deficiencies Identified Letter and return it to RPM**. [Division Director]**

6. Issue the Deficiencies Identified Letter to the applicant, correctly characterize and enter the Deficiencies Identified Letter in the regulatory system and upload it into the administrative file through CBER Connect. **[RPM]**

F. Review Tasks Prior to Mid-Cycle Meeting

1. Confirm the Mid-Cycle Meeting is scheduled via Microsoft Outlook. **[RPM]**

2. Confirm that the PeRC meeting is scheduled, as applicable. **[RPM]**

   a. Review the PeRC Scheduling Process document on FDA's PeRC Information Page website.

3. Determine if a change in review schedule from standard to priority is necessary. **[Review Committee Members]**

   a. Notify applicant within three business days of making the decision, ensure the communication is correctly characterized and entered into the regulatory system and uploaded into the administrative file. **[RPM]**

      i. If there is an upcoming meeting with the applicant, the decision should be discussed during the meeting and included as part of the meeting summary.

      ii. If the applicant is notified via telecon, the telecon summary will be sent to the applicant.

4. If a priority review voucher was requested, ensure that the eligibility criteria have been reviewed. **[Review Committee Members]**

5. Review the Formal Communication Plan agreed to during the pre-BLA/NDA Meeting for any necessary revisions. **[Review Committee Members]** Note: Because Formal Communication Plans are optional, the submission may not have one. Refer to *R 910.05: Formal Communication Plan for Interactions*

and Information Exchange between the Applicant and FDA during Review of an Original BLA or NME NDA for additional information.

6. Continue review activities in preparation for the Mid-Cycle Meeting. **[Review Committee Members]**

a. Refer to *SOPP 8101.5: BLA/NDA Mid-Cycle Meetings and the Mid-Cycle Communication Telecon* for additional information.

b. Each reviewer is expected to document their review of assigned areas in a primary discipline review memorandum that summarizes content, documents the reviewer's assessment, and identifies issues with information and data in the application to date.

c. Prepare a Reviewer Report using information taken from the primary discipline review using the *T 910.09: Reviewer Report* template.

d. Send the Reviewer Report to the RPM (include the Chair and reviewer's immediate supervisor (branch/laboratory chief) no later than four business days prior to the meeting.

7. Lot Release (for products subject to lot release):

a. See *SOPP 8408.1: Development of Laboratory Quality Product Testing Plans and Release of Lots as Part of the BLA Approval Process* for additional information regarding this process.

b. Determine if CBER will conduct any testing of the product "in support" of the application. **[Review Committee Members].**

c. Request that the applicant identify the lots that will be used for testing if not already stated in the application. Determine if any new instrumentation and/or testing personnel training is needed. Communicate the requirements for submission of samples and lot-specific data to the applicant. **[RPM, Chair, DBSQC, and Product Release Branch (PRB)]**

d. Discuss the potential of launch lots with the manufacturer. **[Chair]**

e. Determine, after collaboration, the post-licensure manufacturer's lot release protocol requirements for products subject to lot release or surveillance. **[CMC Reviewer/Product Lead, Chair, DPSQC or LIB, PRB, Statistical Reviewer]**

f. Propose any post-licensure CBER confirmatory lot release testing. **[CMC Reviewer/Product Lead and DBSQC or LIB]**

g. Draft and circulate a Product Testing Plan for review. **[DBSQC or LIB]**

8. Proprietary Name Review:

a. Ensure that the APLB proprietary name review (PNR) memorandum is finalized, correctly characterized and entered in the regulatory system, and uploaded into the administrative file through CBER Connect. **[APLB]**

b. Notify the applicant regarding the PNR decision by the milestone due date. Correctly characterize and enter the communication in the regulatory system, and upload it into the administrative file through CBER Connect. **[RPM]**

c. Refer to *SOPP 8001.4: Review of Proprietary Names for CBER Regulated Products* and *JA 910.02: Proprietary Name Review (PNR) Processing* for additional information.

9. Inspections:

a. If not determined during the first committee meeting, follow up on the need for facility inspections; write inspection waiver memorandum(s) if appropriate. **[OCBQ/DMPQ Reviewer] Note:** Refer to *SOPP 8410: Determining When Pre-License/Pre-Approval Inspections are Necessary* for more information.

b. If not determined during the first committee meeting, follow up on the need for BIMO inspections, confirming sites as needed and issuing inspection assignments to OII, if applicable. **[OCBQ/BIMO Reviewer]**

c. If an inspection is warranted, notify the applicant of our intent to inspect the manufacturing facility at least 60 days in advance of the inspection and no later than mid-cycle. **[OCBQ/DMPQ Reviewer or OCBQ/BIMO Reviewer]**

G. Internal Mid-Cycle Meeting

1. Draft the Internal Mid-Cycle Meeting Agenda using the *T 910.06: Mid-Cycle Meeting Agenda/Summary* template. If a BLA Pre-License Inspection or NDA Pre-Approval inspection has been deemed necessary, the agenda should include a comment regarding communication of our intent to inspect the manufacturing facility at least 60 days in advance of the inspection and no later than mid-cycle. Distribute the agenda and Reviewer Reports to the Mid-Cycle Meeting attendees no later than two days prior to the meeting. **[RPM]**

2. Conduct the Internal Mid-Cycle meeting using *T 910.06: Mid-Cycle Meeting Agenda/Summary*. **[Chair]**

a. Refer to *SOPP 8101.5: BLA/NDA Mid-Cycle Meetings and the Mid-Cycle Communication Telecon* for additional information.

3. Draft the Mid-Cycle Meeting Summary, using information from the agenda sent before the meeting and circulate it to all attendees. **[RPM]**

a. Note for products applicable to the PDUFA/BsUFA Programs: The internal Mid-Cycle Meeting Summary contains the draft agenda for the Mid-Cycle Communication Telecon with the applicant.

4. Review, comment and provide concurrence on the Internal Mid-Cycle Meeting Summary. **[Review Committee Members/Division Director, as applicable]**

5. Correctly characterize the internal Mid-Cycle Meeting Summary in the regulatory system and upload it into the administrative file. **[RPM]**

H. Mid-Cycle Communication Telecon

1. Refer to *R 910.02: Attendee Table for BLA/NDA Meetings* for required attendees. **[RPM]**

a. Mid-Cycle Communication Telecons apply to applications that qualify under the PDUFA/BsUFA Programs.

b. Review Committee Members are included as attendees if they have review discipline issues to discuss.

c. Refer to the *T 910.08: Mid-Cycle Communication (MCC) Telecon Agenda/Summary* template for additional information.

2. Hold the Mid-Cycle Communication Telecon within 2 weeks following the internal Mid-Cycle Meeting to provide an update on the status of the review of the application. **[RPM, Chair]**

3. Provide the Mid-Cycle Communication Telecon agenda (drafted during the internal Mid-Cycle Meeting) to the applicant two business days before the meeting. If there are no issues to discuss, the Mid-Cycle Communication meeting can be cancelled at the request of the applicant. **[RPM, Chair]**

4. Draft and circulate the Mid-Cycle Communication Telecon summary to Review Committee Members ensuring that the content is focused only on the status of the review and any agreements or decisions made. **[RPM]**

5. Review and comment or concur, as appropriate, on the Mid-Cycle Communication Telecon Summary. **[Review Committee Members who participated in the Telecon]**

6. Finalize the Mid-Cycle Communication Telecon Summary and send it to the Product Office Division Director for signature. **[RPM] Note:** In most cases, the DD of the Chair signs the Mid-Cycle Communication Telecon Summary.

7. Sign the Mid-Cycle Communication Telecon Summary and return it to RPM. **[Product Office Division Director]**

8. Issue the Mid-Cycle Communication Telecon summary to applicant, correctly characterize and enter the information for the Mid-Cycle Communication Telecon in the regulatory system and upload it into the administrative file. **[RPM]**

I. Review Continued

1. Continue drafting the primary discipline review**. [Review Committee Members]**

2. Send Information requests, as needed, to facilitate review per *SOPP 8401.1: Issuance of and Review of Responses to Information Request Communications to Pending Submissions*, ensuring that they are correctly characterized in the regulatory system and uploaded into the administrative file. **[RPM, Review Committee Members] Note**: Per *SOPP 8401.1*, information request communications should include the four essential components of Four-Part Harmony:

   a. What was provided – acknowledgement of the information submitted by the applicant, including references to sections, page numbers, or tables where appropriate.

   b. What is the issue or deficiency – identification of a specific issue or concern with information that was submitted, is missing, or is inadequate.

   c. What is needed – explicit request for additional information needed to address the issue and potential alternate ways of satisfying the issue, if applicable.

   d. Why it is needed – statement of basis for the deficiency that includes:

      i. Effect or impact of the specific issue or concern on the patient or marketing application decision, and

ii. Specific reference[1] (when available, applicable, and relevant).

Additionally, IR communications should not be sent late in the review cycle.

3. Prepare and submit PeRC forms, including: **[Clinical Reviewer, Chair]**
- **a.** Pediatric Page
- **b.** Pediatric Template
- **c.** Pediatric Assessment (as appropriate)
- **d.** Pediatric Waiver (as appropriate)
- **e.** Pediatric Deferral (as appropriate)
- **f.** Pediatric Plan (must be included with deferrals)
- **g.** Draft labeling
- **h.** Draft action letter language stating the pediatric disposition
- **i.** Refer to the PeRC Information Web Page (located on FDA's SPO) for additional information**.**

4. Participate in PeRC presentation. **[Clinical Reviewer, Chair]**

5. Ensure that the clinical reviewer has addressed the PREA determination (including waiver/deferrals) and the basis for the decision is reflected in the final clinical review memorandum. **[Clinical Reviewer, Chair]**

6. Notify CBER's Safety Working Group (SWG) Office Representative of any Title IX PMRs and/or safety-related PMCs as needed. **[Office SWG Representative]**

- **a.** Work with SWG Executive Secretary to schedule presentation at the SWG meeting, if needed. **[Office SWG Representative]**

- **b.** Send the proposed PMR(s)/ safety-related PMC (s) language and supportive documentation (i.e., presentation slides) to the SWG Executive Secretary. **[SWG Office Representative]**.

- **c.** Present proposed Title IX PMR(s)/safety-related PMC(s) at the SWG meeting, if applicable. **[OBPV DPV Reviewer, Clinical Reviewer]**

- **d.** Revise the proposed Title IX PMR(s)/safety-related PMC(s) as necessary based on SWG feedback. Schedule additional meetings as necessary. **[Chair, RPM, Clinical Reviewer, OBPV DPV Reviewer]**

7. Notify the applicant of all proposed PMRs (Title IX, PREA, Accelerated Approval, Animal Rule), clinical, safety-related, and non-clinical PMCs and request the applicant's feedback or concurrence. **[RPM]** With respect to

[1] A specific reference is an applicable section of a final rule, regulation, or statute; applicable section of a final guidance; and/or applicable section of an FDA-recognized consensus standard (unless the entire or most of the rule, regulation, statute, or document is applicable).

PDFUA PMR communication dates, please refer to *SOPP 8415: Procedures for Developing Postmarketing Requirements and Commitments.*

a. Using *T 910.04: [8-] OR [6-] Week Postmarketing Requirement (PMR) [and Postmarketing Commitments (PMCs)] Communication*:

i. For standard NME NDAs and original BLAs, communicate details on any anticipated PMRs no later than 8 weeks before the PDUFA action goal date.

ii. For priority NME NDAs and original BLAs, communicate details on any anticipated PMRs no later than 6 weeks before the PDUFA action goal date.

8. Upon applicant's acknowledgement/agreement of PMR/PMC language, provide the final version to Review Committee Members, Office PMR/PMC Coordinator, and supervisor. **[RPM]**

9. Complete the draft Product Testing Plan and send it to the Chair for review. **[DBSQC Chair, CMC Reviewer]**

10. Ensure that the Pharmacovigilance Plan is adequate, if applicable. **[OBPV DPV Reviewer]**

11. Ensure that Establishment Inspection Waiver Memorandum(s) have been completed, correctly characterized, entered in the regulatory system, and uploaded into the administrative file, as needed. **[DMPQ, CMC Reviewers]**

12. If an Environmental Assessment (EA) was submitted, ensure that it has been reviewed and that the review is documented as recommended in *SOPP 8024: Procedures for Environmental Assessments and Claims of Categorical Exclusion*. **[Product Office]**

13. Ensure that the Components Information Table is included in the discipline review memo. **[CMC Reviewer]**

14. If a Categorical Exclusion (CE) claim is included, ensure that its review is documented. Refer to *SOPP 8024: Procedures for Environmental Assessments and Claims of Categorical Exclusion* for instructions for reviewing and documenting the CE. **[Chairing Office]**

15. If reference product exclusivity was requested, ensure that it has been reviewed. Refer to *T 846.02: Reference Product Exclusivity Period Determination Review.* **[CMC Reviewer]**

16. Inspections

a. Perform inspections, if not already completed. **[Review Committee Members, Inspection Team]**

b. Enter inspection memo(s) date(s) in the appropriate regulatory system and upload through CBER Connect if facility inspections were performed. **[DMPQ Lead Inspector]**

c. Send the appropriate sections of the EIR to the respective inspection lead and finalize the report. **[Lead Inspector, CMC Inspector] Note:** EIRs must be completed regardless of final action.

d. Review FDA Form-483 responses as they arrive. If the response(s) is/are complete and adequate, issue memo(s) with supervisory approval to close out the inspection**. [Lead Inspector, CMC Inspector]**

17. Lot Release (for products subject to lot release)

a. Identify the post-licensure lot release protocol review(s) per *SOPP 8408.1: Development of Laboratory Quality Product Testing Plans and Release of Lots as Part of the BLA Approval Process*. **[DBSQC or LIB Representative, CMC Reviewer & Lab Chief, OCBQ/DMPQ/PRB Chief]**

b. Develop Data Collection Plan(s) for Lot Release Protocols. **[Lot Release Protocol Reviewer(s)]**

c. Enter Data Collection Plan(s) into the appropriate regulatory system and upload through CBER Connect. **[Lot Release Protocol Reviewer(s)]**

18. Labeling

a. Schedule labeling meeting(s) as needed. Refer to *SOPP 8412: Review of Product Labeling* for additional information. **[RPM]**

i. Prepare the labeling meeting summary and enter it into the regulatory system. **[RPM] Note:** If appropriate, revised labeling may substitute for a meeting summary.

b. Communicate with the applicant regarding labeling decisions. **[RPM]**

c. If a priority review voucher has been requested and the proposed indication is significantly modified, confirm the change does not impact the PRV process. **[Chair, Clinical Reviewer, RPM]**

J. Late-cycle Meeting for Applications Subject to the PDUFA/BsUFA Programs

1. Update the Reviewer Report from the Mid-Cycle Meeting; send it to the RPM and Chair four days prior to the Internal Late-Cycle Meeting. **[Review Committee Members]**

2. Draft the Late-Cycle Review Committee Memo in preparation for the Internal Late-Cycle Meeting. **[Chair, RPM]**

a. Refer to *SOPP 8101.6: Late-Cycle Meetings* for additional information.

3. Prepare and send the Late-Cycle Internal Meeting agenda, including the Review Committee Memo, to the Review Committee two days before the Internal Late-Cycle Meeting using the *T 910.10: Late-Cycle Meeting (LCM) Internal (Pre) Meeting Agenda/Summary* template. **[Chair, RPM]**

a. Refer to *R 910.02: Attendee Table for BLA/NDA Meetings* to determine the required attendees.

4. Hold the internal Late-Cycle Meeting. **[Chair, RPM, Review Committee Members]**

5. Draft the internal Late-Cycle Meeting Summary using the agenda sent before the internal meeting and circulate it to all meeting attendees. **[RPM]**

6. Review and comment or concur on the internal Late-Cycle Meeting Summary. **Note:** The Meeting Materials and agenda for the Late-Cycle Meeting with the applicant is part of the meeting summary. **[Review Committee Members, Internal Meeting Attendees]**

7. Finalize the internal Late-Cycle Meeting Summary and Meeting Materials and send it to Chair. **[RPM]**

8. Review and concur on the internal Late-Cycle Meeting Summary and Meeting Materials and send them to the Division Director. **[Chair]**

9. Sign the internal Late-Cycle Meeting Summary and the Meeting Materials Cover Sheet and send them to RPM. **[Division Director]**

10. Issue the Late-Cycle Meeting Materials to the applicant no later than ten calendar days (or two calendar days for expedited reviews) before the meeting. If there are no issues to discuss, the Late-Cycle meeting can be cancelled at the request of the applicant. **[RPM]**

11. Correctly characterize, enter the internal Late-Cycle Meeting Summary and Late-Cycle Meeting Materials into the regulatory system and upload them into the administrative file. **[RPM]**

12. Late-Cycle Meeting with Applicant

a. Conduct the Late-Cycle Meeting with the applicant. **[RPM, Chair]**
Note: This meeting is not intended to discuss the pending regulatory decision on the application.

b. Discuss with the applicant whether additional data or analysis that may be submitted will be reviewed by the Agency in the current review cycle and, if so, whether the submission will be considered a major amendment and trigger an extension of the user fee goal date. **[Chair, RPM, Review Committee Members]**

c. Draft the Late-Cycle Meeting Summary using the information from the agenda sent to the applicant before the meeting and *T 910.12: Late-Cycle Meeting Summary.* **[RPM, Chair]**

d. Circulate the draft Late-Cycle Meeting Summary to all CBER/FDA Late-Cycle meeting attendees and supervisors and ensure that there is agreement on the content. **[RPM]**

e. Review and comment or concur on the Late-Cycle Meeting Summary. **[Review Committee Members, Supervisors]**

f. Finalize the Late-Cycle Meeting Summary and send it for signature. **[RPM]**

g. Sign the Late-Cycle Meeting Summary and send it to RPM. **[Chair, Division Director]**

h. Send the Late-Cycle Meeting Summary to the applicant. **[RPM]**

i. Correctly characterize and enter the Late-Cycle Meeting Summary into the regulatory system and upload it into the administrative file. **[RPM]**

K. Amendments

1. Refer to *SOPP 8405.1: Procedures for Resubmissions to an Application or Supplement* for additional information if the amendment is a resubmission.

2. Electronically receive, process, validate, and load into CBER Connect. Notify the appropriate Office per *DCC Procedure Guide 22: Procedure for Processing, Routing, and Storing Electronic Submissions*. **[ESPM]**

3. Characterize the amendment and enter the short summary in the regulatory system. Select the Review Committee Members to review the amendment. **[RPM]**

    a. If the request for the Proprietary Name Review (PNR) is received separate from the BLA/NDA, notify APLB that the amendment is ready for review.

        i. **Note:** The PNR review clock starts when the amendment is received.

        ii. Refer to *JA 910.02: Proprietary Name Review (PNR) Processing* for additional information.

4. Determine if the amendment should be classified as a major amendment. **[Review Committee Members, Division Director] Note:** There is only one major amendment allowed per review cycle.

    a. Major Amendments:

        i. If the amendment is designated as major, follow the procedures in *SOPP 8402: Designation of Amendments as Major.*

        ii. Notify the applicant using the Major Amendment Acknowledgement Letter. **[RPM]**

        iii. Enter the information in the regulatory system to extend the review clock. **[RPM]**

        iv. Reschedule previously scheduled meetings to accommodate the review extension date, as applicable. **[RPM]**

5. Review the amendment. **[Review Committee Members, Chair, RPM]**

L. Review Wrap-up

1. Finalize the Primary Discipline Review Memo(s) and any review addendums, as appropriate, and route them to supervisory chain for signature. **[Review Committee Members]**

2. Perform secondary discipline review of any Primary Discipline Reviews and any review addendums and send them to Division Director for signature. **[Team Lead, Supervisor]**

    a. Review the primary discipline review memorandum(s).

b. If the decision is to concur with the recommendation, a signature on the primary discipline review memorandum is sufficient.

c. If the decision is to non-concur, document the decision and the reasons in a separate review memorandum. Sign the non-concur memorandum before forwarding to Division Director for signature. **Note:** If a non-concurrence memo was written, notify the RPM and Chair.

3. Sign the Primary Discipline Review Memo(s) after the Secondary Discipline Review was signed by supervisor and return to Review Committee Member. **[Division Director]**

4. Determine if a press release is warranted. **[Chair, RPM, Office Press Liaison]**
Note: A press release may be needed for an important indication or a novel product.

5. Correctly characterize and enter the Final Discipline Review Memo and all addendums into the regulatory system and upload them into the administrative file; notify the RPM and Chair. **[Review Committee Members]**

6. Finalize EIRs, ensuring that the narrative report, supervisory endorsement, and other communications are correctly characterized, entered in the appropriate regulatory system and uploaded into the administrative file. **[Inspection Team]**

7. Verify that the Lead Inspector closes out inspection(s) and uploads the inspection endorsement(s), when possible. **[DMPQ RPM]**
Note: If the inspection cannot be closed prior to approval then the final action must result in a complete response (CR) letter.

8. Send the Inspection Tab, including the EIR with exhibits and attachments, and any other paper communications and amendments, to the Document Control Center (DCC) according to *DCC Procedure Guide #11: Procedure for Filing Pre-License/Pre-Approval Inspection Material*. **[Inspection Team]**

9. Enter date(s) of field management directive (FMD-145) letters that were issued for closed inspections into the appropriate regulatory system. **[OCBQ/DIS]**

10. Perform Complete Response (CR) or approval process per the process below. **[Review Committee Members]**

M. Complete Response (CR) Actions

1. Provide discipline review memorandum and CR letter-ready comments, approved by the supervisory chain, to the Chair and RPM. **[Review Committee Members]**

2. Include any compliance issues and/or pending status of inspections in the CR letter. **[RPM, DMPQ Reviewer]**

3. Draft and circulate the CR letter to Review Committee Members, all appropriate Review Office Branch Chiefs and Division Directors for review and agreement. Refer to CBER's Review Letter Templates in CBER's SPO library for the most recently approved template**. [RPM]**

4. Review and comment or concur on CR letter. **[Review Committee Members, Supervisors]**

5. Collate and finalize revisions for the CR letter and send it to the Office Director for signature. **[RPM, Chair]**

6. Sign the CR letter and send it to the RPM. **[Product Office Director]**

7. Ensure that all documents or communications and all other relevant information are correctly characterized and entered into the regulatory system and uploaded into the administrative file. **[Review Committee Members]**

8. Notify the applicant of the CR decision, issue the letter, correctly characterize and enter it into the regulatory system, and upload it into the administrative file. **[RPM]**

9. When a response to the complete response has been received, refer to *SOPP 8405.1: Procedures for Resubmissions to an Application or Supplement***. [Review Committee]**

N. Approval Actions

1. Ensure that the product dating has been determined (expiration dates have been established), if applicable. **[Chair, CMC Reviewer]**

2. Ensure that the labeling comments were communicated to the applicant and final labeling issues were addressed. **[RPM]**

3. Ensure that all product characteristic codes and the short summary are correctly entered, and all necessary fields are completed in the appropriate regulatory system. **[RPM]**

4. If an applicant requested a PRV to be issued or redeemed a PRV for the review of the application, confirm the PRV is processed. **[RPM]**

5. Draft the Summary Basis of Regulatory Action (SBRA) using *T 910.07: Summary Basis of Regulatory Action (SBRA)* and circulate it to Review Committee Members for comment. Refer to *SOPP 8401.10: Processing the Summary Basis of Regulatory Action.* **[Chair]**

6. Review and comment or concur on the SBRA. **[Review Committee Members]**

7. Collate revisions to SBRA and route it to supervisors. **[Chair]**

8. Review and comment or concur on the SBRA. **[Supervisors]**

9. Draft the press release, if needed, and coordinate with the Center Press Release Office. **[Chair or designee]**

10. Draft and circulate the Approval Letter to the Review Committee Members. Please refer to CBER's Review Letter Templates in CBER's SPO Library for the most recently approved template. **[Chair, RPM]**

11. Review and comment or concur on the Approval Letter. **[Review Committee Members]**

a. If the Approval Letter contains any PMR/PMCs, circulate the mature draft to the Office PMR/PMC Coordinator(s) and Center PMR/PMC Liaison for review. **[Chair]**

b. If the approval letter is for a pediatric indication or includes a pediatric indication, ensure the indication listed in the letter matches the indication in the labeling. **[Chair]**

12. Obtain lot release clearance (for products subject to lot release). **[RPM]**

13. Submit final Product Testing Plan to DBSQC or LIB Division Director, Office Director (or designee), DMPQ Director, and Center Lab Quality Manager (CLQM) for signature. **[Chair, DBSQC or LIB Representative]**

14. Enter final Testing Plan information in the regulatory system and upload it through CBER Connect. **[DBSQC or LIB Representative]**

15. Obtain a compliance check (refer to *SOPP 8407: Compliance Check Status* and *JA 900.10: Compliance Check Requests* for additional information). **[RPM, DMPQ RPM]**

16. Obtain a point of contact for the Action Package for Posting requirement from OCOD/Division of Disclosure and Oversight Management (DDOM)/Electronic Disclosure Team (EDT). Refer to *SOPP 8401.7: Action Package for Posting* for additional information. **[RPM]**

17. Send the final draft label revision to the applicant (includes all final Review Committee Member's comments). **[RPM]**

18. Email the Officer/Employee list to all Review Committee Members and those involved in the approval process using *T 910.02: Officer/Employee List Email*. **[RPM]**

19. Respond to the Officer/Employee list email. **[Review Committee Members]**

20. Finalize the SBRA and send it to the Office Director for signature. **[Chair]**

21. Ensure that all communications were correctly entered in the regulatory system and uploaded into the administrative file. **[Review Committee Members]**

22. Perform a quality control review of the CBER generated documents related to the application, ensuring that all documents are in the administrative file, dates are correct, and documents are properly signed; the electronic Action Package (eAP) can be used as a resource. **[RPM]**

23. Send the final draft Approval Letter to all appropriate Review Offices, Branch Chiefs, and Division Directors for review and agreement. **[RPM, Chair]**

24. Review and comment or concur on Approval Letter. **[appropriate review offices, Branch Chiefs, and Division Directors]**

25. Send the Approval letter, SBRA and transmittal memo (*T 910.01: Transmittal Memo*) for signature. **[RPM]** Note: a link to the eAP may be included for Office Director's reference and review during the sign-off process.

26. Sign the Transmittal Memo, SBRA and Approval Letter. **[Office Director(s)]**

a. Signatory Authority for SBRA and Approval Letter

i. Original BLAs (for existing U.S. License Number)/NDAs:
a) Office Director or Deputy Office Director, product office

ii. Original BLAs (for new U.S. License Number)
a) Office Director or Deputy Office Director, product office **AND**

b) Office Director or Deputy Office Director, OCBQ

27. Issue the approval letter and communicate the approval to the applicant. Ensure the approval letter is correctly characterized and entered into the regulatory system and uploaded to the administrative file. **[Chair, RPM]**

28. Provide DMPQ/PRB and DIS/PSB with a copy of the approval letter so that PRB may complete the lot release process and PSB may share the Approval Letter with OII. **[RPM]**

29. Prepare the Action Package for Posting per *SOPP 8401.7: Action Package for Posting* and *C 910.01: Action Package for Posting*. **[RPM]**

30. Provide the Transmittal Memo, the Approval Letter, the Package Insert, the SBRA, and the REMS (if applicable) (in Word format attached to the certified PDF) in an email to OCOD. Refer to *SOPP 8401.7: Action Package for Posting* for additional information. **[RPM]**

31. Complete the Review Completion Process in the regulatory system. **[RPM]**

32. Provide Notification of Release to the applicant for any Launch Lots as appropriate. **[DMPQ review committee member]**

33. Enter PMRs and PMCs into the appropriate regulatory system. **[Office PMR/PMC Coordinator]**

34. Complete electronic Filing Action Package (eFAP) for submission to the Document Control Center (DCC), refer to *DCC Procedure Guide #23: Procedure for Filing Final Action Packages Containing Electronic FDA Communication for Marketing Applications*. **[RPM]**

35. Return any documents (submission file) that need information corrected in the regulatory system. **[DCC]**

36. Make any necessary corrections in the regulatory system. **[Review Committee Members]**

a. For communications not entered prior to the 30-day lockdown, prior approval from the immediate supervisor is necessary for any entries to the regulatory system.

b. Refer to *SOPPJA 910.08: Lockdown of Applicant Submissions and CBER Correspondence for Marketing Submissions* for additional information.

O. After Action Activities

1. Conduct an optional Internal After-Action Meeting to analyze how the review process worked. **[RPM, Review Committee Members]**

   a. Refer to *R 910.02: Attendee Table for BLA/NDA Meetings* for attendees.

   b. Refer to *JA 900.12: After Action Activities for BLAs and NDAs in the PDUFA Program* for additional information.

VIII. Appendix

Not Applicable

IX. References

A. References below are CBER Internal:

1. Document Control Center Procedures
   a. DCC Procedure Guide 8: Procedure for Filing Final Action Packages Containing FDA Correspondence for Marketing Applications
   b. DCC Procedure Guide 11: Procedure for Filing Pre-License/Pre-Approval Inspection Material
   c. DCC Procedure Guide 22: Procedure for Processing, Routing, and Storing Electronic Submissions
   d. DCC Procedure Guide 23: Procedure for Filing Final Action Packages Containing Electronic FDA Communication for Marketing Applications

2. Regulatory Checklists
   a. C 910.01: Action Package for Posting Checklist
   b. C 910.02: 10 Month BLA Checklist
   c. C 910.04: PDUFA Checklist for Original BLAs and Supplements
   d. Discipline Specific Filing Review Checklists

3. Regulatory Job Aids
   a. JA 820.02: Dating of CBER Regulatory Correspondence
   b. JA 900.01: Unique Ingredient Identifier (UNII) Code
   c. JA 900.08: Review of Package and Container Labels
   d. JA 900.10: Compliance Check Requests
   e. JA 900.12: After Action Activities for BLAs and NDAs in the PDUFA Program
   f. JA 910.01: Manufacturing Facility Data Entry
   g. JA 910.02: Proprietary Name Review Processing
   h. JA 910.06: Completing a Filing Review
   i. JA 910.08: Lockdown of Applicant Submissions and CBER Correspondence for Marketing Submissions
   j. JA 910.22: Procedures for Upper Center Management Leadership Briefing Before Issuing a Refuse-to-File (RTF) Letter

4. Regulatory References
   a. R 810.04: Meeting Information
   b. R 810.11: Combination Product Characterization Codes
   c. R 910.02: Attendee Table for BLA/NDA Meetings
   d. R 910.05: Formal Communication Plan for Interactions and Information Exchange between the Applicant and FDA during Review of an Original BLA or NME NDA

5. Regulatory Templates
   a. T 910.01: Transmittal Memo – NDA/BLA/ANDA Originals and Supplements
   b. T 910.02: Officer/Employee List Email
   c. T 910.04: [8-] OR [6-] Week Postmarketing Requirement (PMR) [and Postmarketing Commitments (PMCs)] Communication
   d. T 910.06: Mid-Cycle Meeting Agenda/Summary
   e. T 910.07: Summary Basis of Regulatory Action (SBRA)
   f. T 910.08: Mid-Cycle Communication (MCC) Telecon Agenda/Summary
   g. T 910.09: Reviewer Report
   h. T 910.10: Late-Cycle Meeting (LCM) Internal (Pre) Meeting Agenda/Summary
   i. T 910.11: Late-Cycle Meeting Materials
   j. T 910.12: Late-Cycle Meeting Summary
   k. T 910.15: First Committee Meeting Agenda/Summary
   l. T 910.16: Filing Meeting Agenda/Summary

6. Review Template Letters

7. PeRC Information Page

8. Standard Operating Policies and Procedures (SOPPs)
   a. SOPP 8001.5: Inter-Center Consultative Review Process
   b. SOPP 8024: Procedures for Environmental Assessments and Claims of Categorical Exclusion
   c. SOPP 8101.5: BLA/NDA Mid-Cycle Meetings and the Mid-Cycle Communication Telecon
   d. SOPP 8101.6: Late-Cycle Meetings
   e. SOPP 8401.5: Processing Animal, Biological, Chemical Component Information Submitted in Marketing Applications and Supplements
   f. SOPP 8401.8: Procedures for Consolidating Two STNs (Original Applications of BLAs/NDAs) for the Same Product from the Same Applicant
   g. SOPP 8401.10: Processing the Summary Basis of Regulatory Action
   h. SOPP 8401.12: Study Data Validation Process

B. References below can be found on the Internet:

1. Statutes and Regulations
   a. CFR – Code of Federal Regulations Title 21
   b. Federal Advisory Committee Act (FACA)
   c. Federal Food, Drug, and Cosmetic Act (FD&C Act)
   d. Food and Drug Administration Modernization Act (FDAMA) of 1997
   e. Food and Drug Administration Amendments Act (FDAAA) of 2007
   f. Food and Drug Administration Safety and Innovation Act (FDASIA)
   g. Pediatrics
      i. Pediatric Research Equity Act (PREA)
      ii. Best Pharmaceuticals for Children Act (BPCA)
   h. User Fee Acts
      i. Biosimilar User Fee Act (BsUFA)
      ii. Prescription Drug User Fee Act (PDUFA)

2. Guidance Documents
   a. Guidance for Industry and Review Staff: Good Review Management Principles and Practices for New Drug Applications and Biologics License Applications
   b. Guidance for Industry: Providing Regulatory Submissions in Electronic Format – Certain Human Pharmaceutical Product Applications and Related Submissions using the eCTD Specifications
   c. Guidance for Industry: Providing Regulatory Submissions in Electronic Format – Submissions under Section 745A(a) of the FD&C Act
   d. Guidance for Industry: Expedited Programs for Serious Conditions - Drugs and Biologics
   e. Guidance for Industry: Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees
   f. Guidance for Industry: Information Request and Discipline Review Letters Under the Prescription Drug User Fee Act
   g. Guidance for Industry: Providing Regulatory Submissions in Electronic Format – Standardized Study Data
   h. Guidance for Industry: Advisory Committee Meetings-Preparation and Public Availability of Information Given to Advisory Committee Members

3. Standard Operating Policy and Procedures
   a. SOPP 8001.2: Accessing the FDA Lists of Disqualified and Restricted Clinical Investigators, Debarred Individuals, and Firms Under the FDA Application Integrity Policy
   b. SOPP 8001.4: Review of Proprietary Names for CBER Regulated Products
   c. SOPP 8101.1: Regulatory Meetings with Sponsors and Applicants for Drugs and Biological Products
   d. SOPP 8104: Documentation of Telephone Contacts with Regulated Industry

e. SOPP 8114: Administrative Processing of Documents Received Prior to Submitting Investigational or Marketing Applications (Pre-Application)
f. SOPP 8116: Use of Electronic Signatures for Regulatory Documents
g. SOPP 8119: Use of Email for Regulatory Communications
h. SOPP 8301: Receipt and Processing of Master Files
i. SOPP 8401.1: Issuance of and Review of Responses to Information Request Communications to Pending Submissions
j. SOPP 8401.4: Review Responsibilities for the CMC Section of Biologic License Applications, New Drug Applications and Supplements
k. SOPP 8401.7: Action Package for Posting
l. SOPP 8402: Designation of Amendments as Major
m. SOPP 8404: Refusal to File Procedures
n. SOPP 8404.1: Procedures for Filing an Application When the Applicant Protests a Refusal to File Action (File Over Protest)
o. SOPP 8405.1: Procedures for Resubmissions to an Application or Supplement
p. SOPP 8406: CBER Processing of PDUFA Application Payments
q. SOPP 8407: Compliance Status Checks
r. SOPP 8408.1: Development of Laboratory Quality Product Testing Plans and Release of Lots as Part of the BLA Approval Process
s. SOPP 8410: Determining When Pre-License/Pre-Approval Inspections are Necessary
t. SOPP 8411.1: Administrative Handling and Review of Annual Reports for Approved Biologic License Applications (BLAs)
u. SOPP 8412: Review of Product Labeling
v. SOPP 8413: Postmarketing Requirement/Commitment Related Submissions – Administrative Handling, Review, and CBER Reporting
w. SOPP 8415: Procedures for Developing Postmarketing Requirements and Commitments

4. FDA Forms
   a. Form 356h: Application to Market a New or Abbreviated New Drug or Biologic for Human Use
   b. Form 3397: PDUFA User Fee Coversheet
   c. Form 3674: Certification of Compliance, under 42 U.S.C. §282(j)(5)(B), with Requirements of ClinicalTrials.gov

X. History

Written/Revised	Approved By	Approval Date	Version Number	Comment
Mesarina	Martha Monser, Regulatory Review Document Lead RPOCS, CBER	October 1, 2026	23	• Updates related to consolidating UF program under shared services.

Written/Revised	Approved By	Approval Date	Version Number	Comment
Monser	Martha Monser, RRDL RABOB/DROP/ORO	July 29, 2026	22	• Updated JA 910.16 to SOPP 8401.10
I. Valencia	Katie Rivers, MS Chief, RABOB/DROP/ORO	April 2, 2026	21	• Removed references to S-8430 as it was retired.
Iliana Valencia	Sonday Kelly, MS, RAC, PMP Director, DROP/ORO	November 18, 2025	20	• Added a definition for Smart fill template and updated policy to add use of Smart templates • Added policy for expedited reviews • The steps for the MCM between SOPPs 8101.5 and 8401 were not consistent so this has been corrected • Added the new reference for combination product codes in procedures step 17 • Updated language to add characterizing entries in the regulatory system and uploading to administrative file throughout.
Iliana Valencia	Katie Rivers, MS Chief, RABOB/DROP/ORO	January 15, 2025	19	• Added PRVs and RPE to procedures. • Added AI reviewer to the list of reviewers in procedures. • Added an additional step in procedures that when a CR response is received to refer to SOPP 8405.1. • Added S-8430 to the references section.

Written/Revised	Approved By	Approval Date	Version Number	Comment
Monser/Laughner	Sonday Kelly, MS, RAC, PMP Director, DROP/ORO	January 8, 2024	18	Added new policy regarding consolidating two applications for same product, updated for PDUFA VII PMR/PMC requirements, minor edits for clarification/correction of processes
Monser	Sonday Kelly, MS, RAC, PMP Director, DROP/ORO	September 22, 2023	17	Added new RTF briefing and clarification regarding communications of deficiencies identified during filing review.
Monser	Katie Rivers Chief, RABOB/DROP/ORO	June 30, 2023	16	Clarified that if an application is RTF'd and not FOP, file is closed and a new application would be required.
Martha Monser	Katie Rivers Acting Branch Chief, RABOB/DROP/ORO	February 23, 2023	15	Updates for signatory authority change for CR letters from Division to Office Director
Lynch/Monser Trayer/Ryan	Darlene Martin, MS, PMP ORO/DROP Director, Acting	September 28, 2022	14	Updated for PDUFA VII and BSUFA III
Martha Monser	Christopher Joneckis, PhD	December 13, 2021	13	Updated procedures for study data validation in accordance with JA 900.18 and corrected eAP procedures
Martha Monser	Darlene Martin, MS, PMP	March 7, 2021	12	Update to include JA 910.20 for CE and EA
Martha Monser	N/A	December 11, 2020	11	Technical Update for retirement of EDR and replacement with CBER Connect/CER
Martha Monser	Darlene Martin, MS, PMP	October 22, 2020	10	Updated/clarified procedures regarding inspections and grammatical revisions throughout.

Written/Revised	Approved By	Approval Date	Version Number	Comment
Asia Blackwell	Christopher Joneckis, PhD	February 17, 2020	9	Updated to current policies and aligned procedures with SOPP 8401.2 and the PDUFA Checklist
Dixon	Christopher Joneckis, PhD	September 27, 2017	8	Revised to incorporate new procedures
Rehkopf RMCC Working Group	Robert A. Yetter, PhD	April 18, 2013	7	Revised to accommodate new user fee authorizations and updates from other SOPPs and to add NDAs
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 Yetter, PhD	Oct 2, 2002	3	Changes accommodating PDUFA III and other updates
RMCC	Robert A. Yetter, PhD	Feb 22, 2000	2	Incorporates changes necessitated by publication of BLA final rule (64 FR 56441) and Biostatistics & Epidemiology change from Division to Office
		Sept 10, 1997	1	Original