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# Manual of Standard Operating Procedures and Policies

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## Regulatory - License Applications

### Collaboration of CBER Offices on Issues Related to the Release Of Pre-Licensing and Routine Lots

SOPP 8408

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#### 1. Purpose

Provides guidance pertaining to collaboration between the Product Release Branch (PRB), Division of Product Quality Control, Office of Compliance and Biologics Quality, and other CBER Offices relative to lots submitted in support of a Product License Application (PLA), or a Biologics License Application (BLA), i.e., pre-licensing lots and to routine lot release.

#### 2. Background

In accordance with 21 CFR 610.2(a), samples of any lot of licensed product, together with the protocols showing results of applicable tests, may at any time be required to be submitted to CBER for review and confirmatory testing. Alternatives to official lot release are allowable under the provisions of Federal Register 58:38771-38773 - Guidance on Alternatives to Lot Release for Licensed Biological Products. In a Federal Register notice (60 FR 63048) published December 8, 1995, the Director, CBER, announced that routine lot-by-lot release by CBER would no longer be required for licensed well-characterized therapeutic recombinant DNA-derived and monoclonal antibody biotechnology products.

For pre-licensing lots, the applicant shall identify in the PLA/BLA submission the lot numbers of product which are available for submission to CBER upon request. Failure to identify such lots may be considered as a basis for issuance of a Refusal to File letter to the sponsor.

#### 3. Policy

The timely review of test results and sign-off on lot release protocols are an important part of the approval process for biologicals. Early communication and collaboration is essential during the approval process with respect to review of test protocols, sample requirements and development of new testing procedures.

#### 4. Procedures

##### **Communication Between the Review Committee and the PRB Concerning Lots Submitted in Support of PLA/BLAs:**

- The committee chair will consult with the PRB early in the PLA/BLA review process to determine requirements for sample and test protocol submissions and to identify Individuals to conduct such testing

and review.

- The committee chair will schedule any testing of exhibit lots with the PRB.
- The regulatory coordinator in the division with product responsibility or the committee chair should document and forward all communications between the committee and the PRB to the regulatory coordinator in the respective applications division for documentation and entry into the RMS.
- Copies of all such communications shall be routed to the Document Control Center (DCC) for inclusion in the PLA/BLA file.
- The committee chair will assure the completion of Forms PRB-101 (Request for Control Tests) and PRB-102 (Determination of Acceptance of Protocols for License Application Reports and Supplements for a Specific Reference Number) within 10 working days of receipt from PRB.
- The Chief, PRB, will assure that all lots submitted in support of an application have been processed and that any necessary testing has been satisfactorily completed. Chief, PRB will document this step on the Licensing Action Recommendation Form before the time of approval. For new products or manufacturing changes, protocols and lot samples should be submitted to CBER only after a reference number has been assigned to the application or supplement.
- Chief, PRB will notify the chair of any valid test failures of lots in support.
- Prior to product approval, the Division Director with product responsibility will advise the Chief, PRB of the review laboratory or personnel who will be responsible for routine lot release (protocol review) post-approval, if applicable. Any routine testing to be performed will also be identified.

#### **Communications with the PLA/BLA Sponsor**

- The committee chair will assure that requirements for sample and protocol submissions are communicated to the PLA/BLA sponsor. The chair, in collaboration with PRB, will determine these requirements including the number of samples.
- The committee chairperson will notify the sponsor that failure to have a lot of product available for release at the time of approval may delay the approval process, if applicable.
- In the case of lot failure, the PRB and/or the committee chair will communicate directly with the sponsor for additional samples, resolutions to testing problems, etc. Copies of all such communications should be routed to the regulatory coordinator for entry into RMS and filing with DCC.

#### **Routine Product Release Process (Division with Product Responsibility and the Division of Product Quality Control)**

- PRB receives a protocol for a lot and a sample from that identical lot from the sponsor/manufacturer.
- PRB will enter lot and protocol information into the computer tracking system.
- PRB will circulate the protocol to the appropriate reviewer using a routing slip. The reviewer will review and sign the route slip and enter the information into the computer, RMS.
- The protocol will be returned to PRB after review by the appropriate laboratories.
- PRB will review the protocol routing slip and computer entries for completeness.
- PRB will give notice of release by facsimile/ phone, and will mail the signed paper copy to the appropriate manufacturer.

- PRB's computer will generate the lot release.
- PRB will retain the protocol for two months after which time PRB will send it to DCC.

**5. Effective Date**

November 19, 1996

**6. History**

<b>Written By</b>	<b>Approved By</b>	<b>Approval Date Date</b>	<b>Version Number</b>	<b>Comment</b>
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