

# **SOPP 8403: Issuance and Reissuance of Licenses for Biological Products**

Version #3

Effective Date: September 21, 2010

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## **I. Purpose**

The purpose of this document is to describe how the Center for Biologics Evaluation and Research (CBER) will issue biologics licenses. It describes the procedures and communications that should take place between the CBER offices when processing and issuing these licenses.

## **II. Scope**

The scope of this document is to provide the background, policies and CBER administrative procedures regarding the issuance of a new license and reissuance of existing biological licenses due to changes to an applicant for biological products.

## **III. Background**

- A. Section 351(a) of the PHS Act, as amended November 21, 1997 (the Food and Drug Administration Modernization Act (FDAMA); Public Law 105-115) mandates, in part, that no person shall introduce or deliver for introduction into interstate commerce any biological product unless a biologics license is in effect for that product.
- B. Under 21 CFR Section 600.3 (t) a manufacturer is defined as any legal person or entity, including an individual, association, corporation or chartered organization, who is an applicant for a license where the applicant assumes the responsibility for ensuring compliance with applicable product and establishment standards. The applicant is not required to perform any of the manufacturing steps, but instead may contract with other firms to perform all or part of the manufacture of the product.
- C. A biologics license shall be issued upon a determination that the establishment(s) and product(s) meet all the applicable requirements.

## **IV. Definitions**

N/A

## **V. Policy**

As of December 20, 1999, all U.S. Licenses issued or reissued have been in the form of a letter that, in general, states that the Food and Drug Administration (FDA) hereby grants

the licensed manufacturer a biologics license to manufacture the particular biological product. FDA will not issue license certificates separate from the approval letter as was the agency practice prior to that date (64 FR 56443).

The letter serves as the functional equivalent of a biologics license within the meaning of section 351 of the PHS Act.

**A. Identification of the License Holder when Issuing Licenses**

1. The use of the term "applicant" applies to all applicants of products licensed by CBER. The applicant name on the Form FDA 356(h) in the Biologics License Application (BLA) will be reflected on the biologics license. If the desired name of the license holder will be different from the name and address given on the Form FDA 356(h), this should be specified in the submission. It does not have to be a location engaged in manufacturing.
2. Only one biologics license number will be issued per applicant, no matter how many licensed products the manufacturer makes. All manufacturing facilities including contract manufacturing facilities must be listed on the 356(h) form and will be identified in the license issuance/reissuance letter.

**B. Reissuance of licenses**

1. When there is a change in the applicant, due to a sale, merger or other change that results in a new or substantial name change for the applicant, a new biologics license number will be issued to the new applicant. A substantial change to a company name would be one that does not have any obvious connection to the previous name. If the name change for the new applicant is a minor change from the existing name, then the Center might consider it unnecessary to issue a new biologics license number.
  - a. As an example, if the applicant changes its name by only adding or changing different indications of corporate structure (Inc, Corp, LTD, LLC, etc), then there would be an obvious connection to the previous name, and this would be considered a minor change. The license would be reissued with the same number using the applicant's new name.
  - b. If, however, the applicant changes its name and it has no connection with or includes part of the previous applicant's name, a new license number would be issued.
2. Whenever a license is reissued, the old license(s) will be revoked. The revocation date of the old license(s) will be the same date as the reissuance date of the new license. Pending supplements of the previous license holder will be transferred to the new license holder, if appropriate.

3. When there are changes to the facilities, manufacturing process and procedures, and responsible personnel with no change in the license holder (same applicant), the license number will not be affected. New manufacturing facilities should normally be reported as described in 21 CFR 601.12(b).

**C. License and Product Revocations**

1. Voluntary revocation of a biologics license (or location on a license) may be requested by the license holder (applicant).
2. Requests for the revocation of a biological product should be submitted to CBER as a product correspondence to the appropriate responsible product office.
3. Voluntary revocation of a licensed biological product may be requested by the license holder (applicant) and submitted to the appropriate responsible product office. In general, such revocation should only be considered once all product in distribution has expired. Please note that if an applicant requests revocation of all of their licensed biological products, their biologics license number will also be revoked in accordance with the provisions of Title 21 Code of Federal Regulations 601.5(a)
4. The request for voluntary revocation should include a request to withdraw all pending biologics license application supplements so they can be withdrawn at the time of revocation. The withdrawal request for pending supplements should include a statement that the supplements to be withdrawn do not include changes implemented for product already in distribution. Please note that any pending supplements for which product distribution has already occurred will need to be approved and cannot be withdrawn unless all related product is also removed from distribution.

**D. Checking compliance status when issuing licenses**

Prior to the issuance or reissuance of any license, a check of the compliance status of the applicant should be made by consulting the Division of Case Management, Office of Compliance and Biologics Quality (OCBQ).

**E. Review of Draft Label Changes**

Prior to the reissuance of any license, a review of proposed changes to the labeling will be performed by the product office (21 CFR 610, Subpart G). A review memorandum will be supplied to OCBQ/Division of Manufacturing and Product Quality (DMPQ) for inclusion in the administrative file.

**VI. Responsibilities**

- A. Office of Compliance and Biologics Quality (OCBQ)

1. Division of Case Management (DCM)

Responsible for conducting compliance checks in accordance with CBER *SOPP 8407: Compliance Status Checks*. A satisfactory compliance check must be performed by DCM prior to the issuance or reissuance of a license.

2. Division of Manufacturing and Product Quality (DMPQ)

Responsible for the administrative processing of license reissuance and license revocation requests submitted as product correspondence except for blood and blood components for transfusion and source plasma products.

B. Product Offices

Responsible for the administrative processing of a new licensed biological product, as per CBER *SOPP 8401: Administrative Processing of Biologics License Applications*, label review for any license reissuance, and revoking licensed biological products upon request of the applicant.

VII. **Procedures**

A. **New biologics license issuance**

1. The appropriate division of the Office with product responsibility is responsible for issuing the approval letter. The letter will state that FDA hereby grants the licensed manufacturer a biologics license to manufacture the particular biological product. No biologics license certificate will be issued.
2. Biologics license approval letters for *new license* holders are signed by the Director of the office with product review responsibility and the Director, Office of Compliance and Biologics Quality. The approval letter date serves as the effective date for the new license number.
3. Biologics license approval letters for *new products* for an applicant that already holds an active biologics license number are signed by the Director of the office with product review responsibility.
4. Licensing action letters for blood and blood components for transfusion and source plasma are signed by the Director, Office of Blood Research and Review (OBRR).
5. The biologics license approval letter will be prepared by the Office with product responsibility. The letter will identify the product(s) and manufacturing location(s) covered under the licensing action.
6. The division responsible for preparing the biologics license approval letter will make the appropriate entries including all manufacturing facilities locations and registration numbers into the appropriate CBER regulatory database.

7. Prior to the reissuance of any license, a review of proposed changes to the labeling is performed by the product office (21 CFR 610, Subpart G). A review memorandum is placed in the administrative file.

## **B. Reissuance of license due to changes in the applicant**

1. When the applicant changes their name and a new license needs to be issued:
  - a. DMPQ prepares the biologics license reissuance letter in consultation with the appropriate division(s) in the Office(s) having product responsibility. This also includes the Center for Drug Evaluation and Research (CDER) when an applicant has licensed biological products regulated by both Centers.
  - b. DMPQ coordinates all communications with the applicant related to action on the request.
  - c. If revised draft labeling has not been submitted, DMPQ should request this from the applicant and forward it to the application division with product responsibility.
  - d. The biologics license reissuance letter will state the period of time that the license holder has to submit final versions of the new labeling, usually 180 days from the date of the letter.
  - e. The Office of Blood Research and Review (OBRR), Division of Blood Applications (DBA) will prepare the new biologics license reissuance letter for blood and blood components for transfusion and source plasma.
  - f. The submission provided should include the following in the cover letter: the new name, any changes in personnel, manufacturing, standard operating procedures and manufacturing facilities.
  - g. If the applicant is changing their name due to a corporate buy out, there will need to be two submissions. One submission should be from the applicant being bought. In addition to the information in (f), the cover letter should include information on who is buying the applicant. The other submission should be from the firm buying the applicant. In addition to the information in (f), the cover letter should include information on the applicant they are buying and the products that are being bought, along with a copy of the draft labeling showing the new corporate name and logo. Ideally the submissions should be coordinated so that they can be processed at the same time.
2. When the applicant changes their name but a new license number does not have to be issued, the same procedures as above are followed.
3. All submissions for a new license should include draft labeling that is in color and reflects the new applicant's name. If applicable, where the license number would appear place XXXX. The new license number (if needed) will be issued at the time of approval which will replace the XXXX on draft labeling.
4. These submissions will be handled as product correspondence and will not have a review clock nor will a STN assignment/acknowledgement letter be sent out. If there any questions or inquiries about the name change submissions(s) you may contact OCBQ/DMPQ directly.

5. The letter used to reissue a license due to a change in the applicant will identify all products and manufacturing locations, including contract manufacturing locations, covered under the license. If the name change is due to a corporate buy out, two letters will be issued. One will be to the applicant being bought, revoking their current license number. Another letter will be sent to the firm buying the applicant stating the approval and issuing the new license number. Acknowledgment of receipt of the letter(s) is requested by CBER.
6. The letter will be signed by:
  - a. The Director, OCBQ and the Director of the Office(s) with product responsibility for most biologics products.
  - b. The reissuance letter for blood and blood components for transfusion and source plasma will be signed by the Director, Office of Blood Research and Review (OBRR).
  - c. If licensed products are regulated by both CBER and CDER, then the appropriate representative from CDER would also sign the letter.
7. Pending supplements will be transferred from the old license number to the new license number.

#### **C. Revocation or addition of a manufacturing location**

1. The letter from the applicant used to acknowledge the voluntary revocation of a manufacturing location(s) will identify all products and manufacturing locations covered under the license for which authorization to introduce or deliver for introduction into interstate commerce remains within the scope of the biologics license.
2. Pending supplements which are tied to a location undergoing revocation must either be withdrawn by the firm or transferred to locations covered under the license, when feasible.
3. The revocation of a manufacturing location(s) will be indicated in the letter to the applicant.
4. The addition of a manufacturing location(s) will require submission and approval of a prior approval supplement or supplements, and the approval letter for the supplement will constitute the biologics license documentation for the addition of the new manufacturing site(s).
  - a. These letters will be signed by the Director, Office of Compliance and Biologics Quality (OCBQ), with the exception of blood and blood components for transfusion and source plasma. The reissuance letter for these products will be signed by the Director, Office of Blood Research and Review (OBRR).

#### **D. Change in product name**

1. These reissuances will be the responsibility of the appropriate division in the Office with product responsibility, and they will coordinate all communications with the applicant related to action on the request. A reissuance of this kind will require only a letter issued by the office with

product responsibility.

**E. Checking compliance status when issuing licenses**

1. Prior to the issuance or reissuance of any license, a check of the compliance status of the applicant should be made by consulting the OCBQ/DCM.
2. If the applicant is undergoing integrity review, prior to the licensing decision, the product review office will confer with the OCBQ/DCM in accordance with CBER *SOPP 8407: Compliance Status Checks*.

**F. Review of Draft Label Changes**

1. Prior to the reissuance of any license, a review of proposed changes to the labeling will be reviewed by the product office for significant concerns related to labeling standards (21 CFR 610, Subpart G) . A review memorandum will be supplied to OCBQDMPQ for inclusion in the administrative file.

**VIII. Appendix**

N/A

**A. References**

- A. 63 FR 40858-40871, July 31, 1998.
- B. 64 FR 56441-56454 (56443), October 20, 1999
- C. SOPP 8407: Compliance Status Checks
- D. SOPP 8401: Administrative Processing of Biologics License Applications (BLA)

**X. History**

<b>Written / Revised By</b>	<b>Approved By</b>	<b>Approval Date</b>	<b>Version Number</b>	<b>Comment</b>
OCBQ/DMPQ	Robert A. Yetter, PhD	September 14, 2010	#3	Incorporates administrative changes handling related to license numbers

<b>Written / Revised By</b>	<b>Approved By</b>	<b>Approval Date</b>	<b>Version Number</b>	<b>Comment</b>
<b>RMCC</b>	Rebecca Devine	April 6, 1999	#2	Incorporates changes resulting from creation of Office of Compliance and Biologics Quality and revisions to 21 CFR 600.3(t) and 601.2(c).
<b>CBER Application Policy Task Force</b>	M. Beatrice	September 10, 1993	#1	OD-R-3-93 reissued as SOPP 8403 in August 1997. No change to Guide content.

## References

- [SOPP 8407: Compliance Status Checks](#) Effective Date: Date: November 28, 2006
- [SOPP 8401: Administrative Processing of Biologics License Application \(BLA\)](#) Effective Date: May 1, 2007