

SOPP 8403: Issuance, Reissuance, and Voluntary Revocation of Biological Products Licenses

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I. Purpose

- A.** This Standard Operating Policy and Procedure serves as a guide for the Center for Biologics Evaluation and Research (CBER) staff to describe:
1. The process for issuing biologics licenses for new biological products and/or to applicants,
 2. How changes to applicants or ownership of biological products will be administratively handled and reviewed (i.e., reissuance), and
 3. The process for the voluntary revocation of a U.S. License No., including a biological product under an existing license, or a manufacturing location under the license.
- B.** The SOPP also describes the procedures and communications that should take place between CBER offices when processing and issuing these licenses.

II. Scope

This SOPP applies to biological products regulated under section 351 of the Public Health Service Act.

III. Background

- A. Section 351(a) of the Public Health Service (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. A biologics license may be issued or reissued when there is a change to the applicant only upon a determination that the establishment(s) and product(s) meet all the applicable requirements.
- C. A biologics license may be revoked upon voluntary withdrawal of the product from the market and/or transfer of the product(s) to a new applicant.

IV. Definitions

- A. **Manufacturer** - Any legal person or entity engaged in or responsible for the manufacture of a drug or device, including biological products subject to the Food, Drug, and Cosmetic Act or license under the Public Health Service Act (PHSA). "Manufacturer" also includes any legal person or entity who is an applicant or named in an application, whereby the applicant assumes responsibility for compliance with the applicable product and establishment standards.

V. Policy

- A. Since December 20, 1999, all U.S. Licenses issued or reissued have been in the form of an approval letter that, in general, states that the Food and Drug Administration (FDA) hereby grants the manufacturer (i.e., the applicant) a biologics license to manufacture and commercially distribute the particular biological product (64 FR 56443).
- B. The approval letter serves as the functional equivalent of a biologics license within the meaning of section 351 of the PHS Act.
- C. Changes to a U.S. License that are required due to changes to the applicant's or the product's ownership will be handled as administrative actions through product correspondence. The information regarding the new applicant

including changes to the labeling will be reviewed by the responsible product office.

- D. If a product (or products) is/are being transferred to a new applicant, the information supplied by the current applicant for voluntary revocation of the license(s) will also be reviewed, and revocation will be coordinated to take place at the same time the license issues to the new applicant.
- E. Revocation of a single biologics license will be handled by the appropriate product office.

F. Identification of the License Holder and information included in Licensing letters:

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), specify this in the submission. The location of the applicant does not have to be engaged in manufacturing.
2. Only one U.S. License No. will be issued per applicant, regardless of how many licensed biological products are owned by the applicant.
3. All manufacturing facilities, including contract manufacturing facilities, must be listed on the 356(h) form and will be identified in the U.S. License issuance/reissuance letter.

G. Reissuance of licenses

1. Requests for reissuance of a U.S. License No. will be handled as product correspondence and will not be under a review clock nor will an STN assignment/acknowledgement letter be sent. For questions or inquiries about the name change submissions(s), contact the office processing the change.
2. The submission for a change in applicant or product ownership should include the following in the cover letter: the new applicant name, any changes in personnel, manufacturing, standard operating procedures and manufacturing facilities.
3. If the name change is due to a corporate buy out, two submissions are needed.

- a. One submission should be from the applicant being bought. In addition to the information in (G3), the cover letter should include information (e.g., name, address, existing License No, if applicable) on who is buying the applicant.
 - b. The other submission should be from the firm buying the applicant. In addition to the information in (G3), the cover letter should include information (e.g., name, address, license No., if applicable) on the applicant they are buying and the products that are being bought.
 - c. Ideally, the submissions should be coordinated so they can be processed at the same time.
4. All pending supplements will be transferred from the old US License No. to the new U.S. License No..
5. 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 License holders name, an administrative review of the information will be conducted and a new U.S. License No. 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 CBER might consider it unnecessary to issue a new U.S. License No.
 - a. As an example, if the applicant changes its name by only adding or changing the nature of the corporate entity (Inc, Corp, Ltd, LLC, etc.), then there is an obvious connection to the previous name, and thus would be considered a minor change. The U.S. License No. would be reissued with the same number using the applicant's new name.
 - b. If, however, the applicant changes its name and it has little to no connection with or includes only a limited amount of the previous applicant's name, a new U.S. License No. would generally be issued.
6. Whenever a U.S. License No. is reissued, the old U.S. License No(s) will be revoked. The revocation date of the old will be the same date as the reissuance date of the new U.S. License No. Pending supplements of the previous US license holder will be transferred to the new US license holder, if appropriate.

H. License and Product Revocations

1. Voluntary revocation of a U.S. License No. (to include all products under the license) may be requested by the U.S. license holder (applicant).

- a. If an applicant requests revocation of all of their licensed biological products, their U.S. License No. will also be revoked in accordance with the provisions of 21 CFR 601.5(a), (see H1).
 - b. Requests for revocation of a manufacturing location under the US License No. are reviewed by the Division of Manufacturing and Product Quality (DMPQ) in the Office of Compliance and Biologics Quality (OCBQ) for all biological products except blood banks and plasma centers which are reviewed by the Division of Blood Components and Devices (DBCD) in the Office of Blood Research and Review (OBRR).
2. The letter from the applicant requesting the voluntary revocation of a manufacturing location(s) will identify all products and manufacturing locations covered under the U.S. License No. for which authorization to introduce or deliver for introduction into interstate commerce remains within the scope of the biological product license.
3. Pending supplements which are tied to a location undergoing revocation must either be withdrawn by the firm or transferred to locations covered under the biologics license, when feasible.
4. Voluntary revocation of a single licensed biological product (STN) may be requested by the license holder (applicant) and reviewed by the appropriate product office.
 - a. In general, such revocation should only be considered once all product in distribution has expired.
5. The request for voluntary revocation of a single biological product license (STN) should include a request to withdraw all appropriate pending supplements so they can be withdrawn at the time of revocation.
 - a. 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.
 - b. 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.
6. In some cases, one or more licensed products from the original applicant may be transferred to a new applicant, with the original applicant still retaining licensed products after the transfer.
 - a. Information regarding the applicants and products would be submitted as noted in Section G above.

- b. Two regulatory letters will need to be sent – a licensing letter to the new applicant that will be assuming responsibility for the product(s) transferred, and a revocation letter to the original applicant revoking the products under their existing license.
- i. The letter to the new applicant for the transferred products will be a licensing letter to transfer the product(s), or a license issuance if the new applicant is currently not a license holder.
- c. The letters to the new applicant and original applicant will be dated so that the new license issuance and old license revocation is effective at the same time.

I. Addition of a manufacturing location

- 1. The addition of a manufacturing location(s) requires the submission and approval of a prior approval supplement(s) (PASs).
- 2. The approval letter for the supplement(s) will constitute the biologics license documentation for the addition of the new manufacturing site(s).

J. Checking compliance status

- 1. A compliance check must be performed prior to the issuance or reissuance of a license for products licensed by CBER. The compliance check is performed to ensure there are no ongoing or pending investigations or compliance actions. See *SOPP 8407: Compliance Status Checks* for further information.
- 2. A compliance status check is not required for requests for revocation.

K. Labeling

- 1. For new products: Prior to the issuance of an approval for a biological product, a review of proposed labeling (21 CFR 610, Subpart G) will be performed by the product office with review responsibility as part of the BLA review. See *SOPP 8412: Review of Product Labeling* for further information regarding label review.
- 2. For existing licensed products: As the reissuance of a U.S. License No. is an administrative review, submission of the revised labeling should only address changes to the applicant, license number, or other administrative changes. There should not be other changes to the labeling (such as changes in prescribing information) submitted as part of a reissuance action.

VI. Responsibilities

A. Office of Compliance and Biologics Quality (OCBQ) Division of Case Management (DCM) - Conducts compliance checks in accordance with CBER's *SOPP 8407: Compliance Status Checks* and *JA 900.10: Compliance Check Requests*.

B. Division of Manufacturing and Product Quality (DMPQ)

1. Administratively processes US License No. reissuance and US License No. revocation requests except for blood and blood components for transfusion and source plasma products.
2. Administratively processes Revocation requests for manufacturing locations under the U.S. License No.
3. Requests compliance checks for license reissuances and product transfers

C. Product Offices

1. Administratively processes biological product (STN) revocation requests revoking licensed biological products upon request of the applicant (when the product is not being transferred to another applicant, and
2. Reviews labeling under the BLA and labeling supplements submitted under 21 CFR 601.12(f), and for the reissuance of licenses.

D. Office of Blood Research and Review (OBRR)/Division of Blood Components and Devices (DBCD)

1. Administratively processes license reissuance and license revocation requests for blood and blood components for transfusion and source plasma products, as well as the revocation of manufacturing locations for these products.
2. Reviews associated labeling for blood and blood components for transfusion and for further manufacturing

E. Office of Communication, Outreach, and Development (OCOD)/ Division of Communication and Consumer Affairs (DCCA)/Communication Technology Branch (CTB)

1. Responsible for preparing for updating information on FDA's Internet Web site.

2. Responsible for communicating with product office RPMs to inform them that the posting has been completed.

VII. Procedures

A. New biologics license issuance

Note: Refer to *SOPP 8401: Administrative Processing of Original Biologics License Applications (BLA) and New Drug Applications* for general information on the review process for new biologics license applications.

1. Prepare the approval letter, using the letter template found in the Letter Templates site on CBER's Review Resources SharePoint hub and send it to the correct signatory authorities. **[appropriate division of the Office with product review responsibility]**
 - a. Note: The letter will identify the product(s) and manufacturing location(s) covered under the licensing action.
2. Complete the compliance status check. Refer to *SOPP 8407: Compliance Status Checks* and *JA 900.10: Compliance Check Requests* for more information. **[DCM]**
3. Sign the approval letter
 - a. Signature authority for biologics license approval letters for **new U.S. License No.** holders:
 - i. Director of the office with product review responsibility **and**
 - ii. Director, OCBQ, if a new License No.
 - iii. Note: The approval letter date serves as the effective date for the new U.S. License No.
 - b. Signature authority for biologics license approval letters for **new products** for an applicant that already holds an active U.S. License No.:
 - i. Director of the office with product review responsibility.
4. Ensure that the appropriate entries, including all manufacturing facilities locations and FEI are entered into the appropriate regulatory system and uploaded into CBER's EDR. **[DMPQ RPM and the Product Office RPM]**

B. Reissuance of U.S. License No.

1. Determine whether or not a new U.S. License No. needs to be issued when the applicant changes their name (see Policy G.5.a.). **[DMPQ, DBCD]**
 - a. Ensure that the submission contains the following information on the cover letter:
 - i. The new name
 - ii. Any changes in personnel, manufacturing, standard operating procedures and manufacturing facilities.
 - b. Complete the compliance status check. Refer to *SOPP 8407: Compliance Status Checks* and *JA 900.10: Compliance Check Requests* for more information. **[DCM]**
 - c. Prepare the U.S. License No. reissuance letter in consultation with the appropriate division(s) in the Office(s) having product responsibility. This consultation includes the Center for Drug Evaluation and Research (CDER) when an applicant has licensed biological products regulated by both Centers. **[DMPQ]**
 - d. Prepare the U.S. License No. reissuance letter for blood and blood components for transfusion and for further manufacturing. **[DBCD]**
 - e. Coordinate all communications with the applicant related to action on the request. **[DMPQ, DBCD]**
 - f. Forward revised draft labeling to the appropriate division with product responsibility for review for the license reissuance. **[DMPQ]**
2. Issue one letter if the name of the applicant has changed due to a corporate buy out, merger, or similar situation that changes the applicant such that either a reissuance of the letter to the same applicant under the existing U.S. License No. or a new U.S. License No. needs to be established.
 - a. In the case where a new applicant's name is not significantly different than the existing applicant name, the letter would be a reissuance of the existing U.S. License No. using the applicant's new name.
 - b. In the case where a new U.S. License No. needs to be issued, the letter would revoke the old U.S. License No. and issue a new U.S. License No.

- c.** Signature authorities for the letter:
 - i.** Director, OCBQ and the Director of the Office(s) with product responsibility (for most biological products),

or
 - ii.** Director, OBRR (for blood and blood components for transfusion and source plasma).
- 4.** Issue two letters if biological products or manufacturing locations are going to be transferred to a new applicant *and* the existing U.S. licensed applicant will still be licensed for biological products that have not been transferred *or* the original applicant is revoking the U.S. License No. with products transferred to a new applicant (not part of a buy out or merger).
[DMPQ or DBCD]
 - a.** Issue one letter to the applicant that is transferring the products. The letter should list all products being transferred or revoked. Note: if the applicant is transferring or revoking all the products under their U.S. License No. the U.S. License will be revoked.
 - b.** Signature authorities for the letter to the applicant:
 - i.** Director, OCBQ and the Director of the Office(s) with product responsibility (for most biologics products).
 - ii.** Director, OBRR (for blood and blood components for transfusion and source plasma).
 - iii.** The appropriate representative from CDER if license products are regulated by both CBER and CDER.
 - c.** Issue another letter to the firm acquiring the transferred products. The letter may be to an existing U.S. licensed applicant to add the additional products, or a new U.S. License No. may be issued if the new applicant is not currently licensed.
 - d.** Request acknowledgment of receipt of the letter(s).
 - e.** Signature authorities for the letter to acquisition firm:
 - i.** Director, OCBQ and the Director of the Office(s) with product responsibility (for most biologics products).

- ii. Director, OBRR (for blood and blood components for transfusion and source plasma).
 - iii. The appropriate representative from CDER if license products are regulated by both CBER and CDER.
5. Transfer pending supplements from the old U.S. License No. to the new U.S. License No.. **[DMPQ or DBCD]**
 6. Ensure that the appropriate entries are entered into the appropriate CBER regulatory system and uploaded into the EDR. **[DMPQ, DBCD]**

C. Revocation of a US license No. or manufacturing location

1. Ensure that the letter from the applicant requesting voluntary revocation identifies all products and manufacturing locations covered under the U.S. License No. for which authorization to introduce or deliver for introduction into interstate commerce remains within the scope of the biological product license (STN). **[DMPQ]**
2. Issue letter for the revocation of a manufacturing location(s) to the applicant. **[DMPQ]**
3. Signature authority for the letter:
 - a. Director, OCBQ for a location;
 - Or
 - b. Both OCBQ and the Product Office Director when the entire US License is being revoked.
4. Ensure that pending supplements for the applicant are withdrawn by the firm or transferred to locations covered under the U.S. License. **[DMPQ]**
5. Ensure that the appropriate entries are entered into the appropriate CBER regulatory system and are uploaded into the EDR. **[DMPQ]**
6. Ensure that CBER's Product Approval Page is updated as needed using the transmittal memo template, T910.01. **[DMPQ and OCOD/DCCA/CTB]**

D. Revocation of a biological product license (STN)

1. Ensure that the letter from the applicant requesting voluntary revocation identifies the biological product(s) covered under the U.S. License for which authorization to introduce or deliver for introduction into interstate

commerce remains with the scope of the biological product license.

[Product Office]

2. Issue the letter for the revocation of the biological product license (STN) to the applicant. **[Product Office]**
3. Signature authority for the letter:
 - i. Director of the Office with product review responsibility
4. Ensure that pending supplements for the applicant are withdrawn by the firm. **[Product Office] Note:** if there are pending supplements notify the applicant to close out those supplements.
5. Ensure that the appropriate entries are entered into the appropriate regulatory system and uploaded into the EDR. **[Product Office]**
6. Ensure that CBER's Product Approval Page is updated as needed using the transmittal memo template, T910.01. **[DMPQ and OCOD/DCCA/CTB]**

VIII. Appendix

N/A

IX. References

A. References below are CBER Internal:

1. JA 900.10: Compliance Check Requests
2. T910.01: Transmittal Memo – NDA/BLA/ANDA Originals and Supplements

B. References below may be found on the Internet:

1. [64 FR 56441-56454 \(56443\), October 20, 1999](#)
2. [SOPP 8407: Compliance Status Checks](#)
3. [SOPP 8401: Administrative Processing of Original Biologics License Applications \(BLA\) and New Drug Applications](#)
4. [SOPP 8412: Review of Product Labeling](#)

X. History

Written / Revised By	Approved By	Approval Date	Version Number	Comment
J. Eltermann	Christopher Joneckis, PhD	October 25, 2020	4	Updated to current procedures.
OCBQ/DMPQ	Robert A. Yetter, PhD	Sept 14, 2010	3	Incorporates administrative changes handling related to license numbers
RMCC	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).
CBER Application Policy Task Force	M. Beatrice	Sept 10, 1993	1	OD-R-3-93 reissued as SOPP 8403 in August 1997. No change to Guide content.