

SOPP 8403: Issuance, Reissuance, and Voluntary Revocation of Biological Product 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.
- 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.
- D. In general, the business process (external to CBER) of product transfers between manufacturers occurs prior to the submission of the notification/request to CBER.

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. License numbers are not provided to the applicant in advance of issuing the approval letter.

- 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's 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 reviewed on a specific review schedule nor will an assignment/acknowledgement letter be issued. For questions or inquiries about applicant name change submission(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's 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.** The first submission should be from the applicant being bought. 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, as an amendment to the original product correspondence, should be from the firm buying the applicant. 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 U.S. License No. to the new U.S. License No., upon license transfer/reissuance.
- 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 holder's 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 may 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.

Note: Applicants may contact CBER/OCBQ to inquire whether the name change will be considered major or minor before submitting the request.

- 6.** Whenever a U.S. License No. is reissued to the same applicant, the old U.S. License No. will be revoked. The revocation date of the old No. will be the same date as the reissuance date of the new U.S. License No.

Any pending supplements under the previous U.S. license holder will be transferred to the new U.S. license holder, as applicable.

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 (the applicant). Prior to revocation of a U.S. License, the firm should confirm that no distributed products remain in circulation and are expired (certain exceptions may apply for cell and gene therapy products).
 - a. If an applicant requests revocation of all their licensed biological products, their U.S. License No. will also be revoked in accordance with the provisions of 21 CFR 601.5(a).
2. Existing postmarketing commitments and/or requirements (PMCs/PMRs) should be released upon revocation of a product; however, the product office will make a final determination dependent upon the specific circumstances related to the PMC/PMRs.
3. Pending supplements which are tied to a license revocation must be withdrawn by the firm.
4. Voluntary revocation of a single licensed biological product 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 distributed product has expired (certain exceptions may apply for cell and gene therapy products).
5. The request for voluntary revocation of a single biological product license 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 distributed product already in circulation.
 - b. Any pending supplements for which distributed product has already occurred will need to be approved and cannot be withdrawn unless all related distributed product is also removed from circulation.

I. Product Transfers and Product Revocations

1. In some cases, one or more licensed products from the original applicant may be transferred to a new applicant, with the original applicant retaining other existing licensed products after the transfer.
 - a. The applicant who is transferring the product should submit a request via product correspondence. In the cover letter, the new applicant should be identified.
 - b. The new applicant should then submit an amendment to the original product correspondence. The cover letter included with this amendment should include the name, address, U.S. License No., and responsible contact of the new applicant. **Note:** any other changes for the new applicant should be submitted as supplements after the product transfer has been completed.
2. Ideally, the submissions should be coordinated so they can be processed at the same time.
3. 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 product(s) under their existing license.
 - a. The letter to the new applicant for the transferred products will be a licensing letter to transfer the product(s). However, if the new applicant is currently not a license holder, it will be a license issuance.
 - b. The letters to the new applicant and original applicant will be dated so that the new license issuance and old license revocation is effective on the same date.
 - c. For product transfers and revocations that do not affect the U.S. License No., the product office is responsible for issuing both letters.

J. Addition of a manufacturing location

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

K. Removal of a manufacturing location:

1. If requesting removal of a manufacturing location, the applicant should submit the request via product correspondence. No changes will be required regarding the U.S. License No.

L. 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.

M. 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. OCBQ/Division of Manufacturing and Product Quality (DMPQ)

1. Administratively processes U.S. License No. reissuance and U.S. License No. revocation requests except for blood and blood components for transfusion and source plasma products.
2. Requests compliance checks for license reissuances and product transfers if they are the responsible office.

C. Product Offices

1. Administratively processes biological product 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. Note: review of labeling associated with product transfers/license reissuance, the review is limited to the changes related to it, e.g., name, license number, etc. Ensures that no other content changes were submitted.
3. Requests compliance checks for requests for which they are the responsible office.

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.
2. Reviews associated labeling for blood and blood components for transfusion and for further manufacturing.

E. Office of Regulatory Operations (ORO)/Division of Informatics (DI)/Regulatory Information Branch (RIB)

1. Completes data entry into CBER regulatory tracking systems required for U.S. License No. reissuance and U.S. License No. revocation requests including blood and blood components for transfusion and source plasma products.
2. Completes data entry into CBER regulatory tracking systems required for revocation requests under the U.S. License No.
3. Updates the Purple Book as needed for license changes.

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

1. Responsible for preparing and 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 Online (SPO) 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.
 - b. Contact RIB to obtain the U.S. License No.
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 U.S. 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 (contact DMPQ if changes are needed) and uploaded into CBER's electronic repository (CER). **[DMPQ RPM and the Product Office RPM]**

B. Procedures related to an applicant's request for a name change

1. Determine if 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 in the cover letter:
 - i. The new name
 - ii. Any changes in personnel, manufacturing, standard operating procedures, and manufacturing facilities.
 - b. Verify if CDER products are affected by the request. If so, coordinate with CDER. **[DMPQ]**
 - c. Forward the draft labeling to the appropriate division with product responsibility. **[DMPQ]**
 - d. Complete labeling review ensuring that the only changes are related to the name change. **[Product Office RPM or designee]**
 - e. Complete the compliance status check. Refer to *SOPP 8407: Compliance Status Checks* and *JA 900.10: Compliance Check Requests* for more information. **[DCM]**
 - f. Prepare the U.S. License No. reissuance letter in consultation with the appropriate division(s) in the Office(s) having product responsibility. **[DMPQ]**
 - g. Contact RIB to obtain the new U.S. License No. **[DMPQ]**
 - h. Prepare the U.S. License No. reissuance letter for blood and blood components for transfusion and for further manufacturing. **[OBRR/RPMS]**
 - i. Coordinate all communications with the applicant related to action on the request. **[DMPQ or OBRR/RPMS]**
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).
3. Transfer pending supplements from the old U.S. License No. to the new U.S. License No. **[DMPQ, DBCD/OBRR or RPMS/OBRR]**
4. Forward the concurrence copy of the letters to RIB. **[DMPQ or OBRR]**
5. Ensure that the appropriate entries are entered into the appropriate CBER regulatory system and uploaded into the CER. **[RIB]**

C. Revocation of a U.S. License No.

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. The letter should also confirm that no distributed product remains in circulation and all products are expired (certain exceptions may apply for cell and gene therapy products). **[DMPQ]**
2. Signature authorities for the letter:
 - a. Both OCBQ and the Product Office Director.
3. Ensure that pending supplements for the applicant are withdrawn by the firm or transferred to locations covered under the U.S. License. **[DMPQ]**
4. Forward the concurrence copies of the letters to RIB. **[DMPQ]**

5. Ensure that the appropriate entries are entered into the appropriate regulatory system and are uploaded into the CER. **[RIB]**
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

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 within the scope of the biological product license. **[Product Office]**
2. Issue the letter for the revocation of the biological product license to the applicant. **[Product Office] Note:** Ensure that all additional instructions on the letter template information page regarding status updates, release of PMRs/PMCs, trans-BLAs, etc. are reviewed and addressed.
 - a. Signature authority for the letter: Product Office Director
3. Ensure that pending supplements for the applicant are withdrawn by the firm. **[Product Office] Note:** if there are pending supplements notify the applicant to request withdrawal of those supplements.
4. Forward the concurrence copies of the letters to RIB. **[Product Office]**
5. Ensure that the appropriate entries are entered into the appropriate regulatory system and uploaded into the CER. **[RIB]**
6. Ensure that CBER's Product Approval Page is updated as needed using the transmittal memo template, T910.01. **[DMPQ and OCOD/DCCA/CTB]**

E. Product revocation and transfers

1. Ensure that the letter from the applicant requesting voluntary revocation/transfer identifies the biological product(s) to be revoked and transferred to a new applicant and identifies the new applicant. **[Product Office]**
2. Ensure that the letter from the new applicant identifies the product(s) and that proposed labeling has been submitted as an amendment to the original product correspondence. **[Product Office]**
3. Review the proposed labeling, ensuring that the only changes are related to the name change. **[Product Office RPM or designee]**

4. Request a compliance check. **[Product Office RPM]**
5. 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). **[Product Office]**
 - a. Issue one letter to the applicant that is transferring the products. The letter should list all products being transferred or revoked.
 - b. Signature authority for the letter to the applicant: Product Office Director
 - 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. Signature authority for the letter to acquisition firm: Product Office Director

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 \(NDA\)](#)
4. [SOPP 8412: Review of Product Labeling](#)

X. History

Written / Revised By	Approved By	Approval Date	Version Number	Comment
M. Monser	N/A	February 27, 2023	6	Technical update for 2023 CBER reorganization.
M. Monser/J. McGuire	Darlene Martin, MS, PMP ORO/DROP Director	November 13, 2022	5	Updated to disassociate STN from biological product license, to clarify data entry responsibilities and clarified policy/procedures related to product transfers and product revocations.
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.