AUTHORITY: 15 U.S.C. 1451–1561; 21 U.S.C. 321, 351, 352, 353, 355, 356b, 360, 360c-360f, 360h-360j, 371, 374, 379e, 381; 42 U.S.C. 216, 241, 262, 263, 264; sec 122, Pub. L. 105–115, 111 Stat. 2322 (21 U.S.C. 355 note), sec 7002(e), Pub. L. 111–148, 124 Stat. 817, as amended by sec. 607, Division N, Pub. L. 116–94, 133 Stat. 3127.

SOURCE: 38 FR 32052, Nov. 20, 1973, unless otherwise noted.

CROSS REFERENCES: For U.S. Customs Service regulations relating to viruses, serums, and toxins, see 19 CFR 12.21–12.23. For U.S. Postal Service regulations relating to the admissibility to the United States mails see parts 124 and 125 of the Domestic Mail Manual, that is incorporated by reference in 39 CFR part 111.

Subpart A—General Provisions

§ 601.2 Applications for biologics licenses; procedures for filing.

(a) *General.* To obtain a biologics license under section 351 of the Public Health Service Act for any biological product, the manufacturer shall submit an application to the Director, Center for Biologics Evaluation and Research or the Director, Center for Drug Evaluation and Research (see mailing addresses in §600.2(a) or (b) of this chapter), on forms prescribed for such purposes, and shall submit data derived from nonclinical laboratory and clinical studies which demonstrate that the manufactured product meets prescribed requirements of safety, purity, and potency; with respect to each nonclinical laboratory study, either a statement that the study was conducted in compliance with the requirements set forth in part 58 of this chapter, or, if the study was not conducted in compliance with such regulations, a brief statement of the reason for the

noncompliance; statements regarding each clinical investigation involving human subjects contained in the application, that it either was conducted in compliance with the requirements for institutional review set forth in part 56 of this chapter; or was not subject to such requirements in accordance with § 56.104 or § 56.105, and was conducted in compliance with requirements for informed consent set forth in part 50 of this chapter. A full description of manufacturing methods; data establishing stability of the product through the dating period; sample(s) representative of the product for introduction or delivery for introduction into interstate commerce; summaries of results of tests performed on the lot(s) represented by the submitted sample(s); specimens of the labels, enclosures, and containers, and if applicable, any Medication Guide required under part 208 of this chapter proposed to be used for the product; and the address of each location involved in the manufacture of the biological product shall be listed in the biologics license application. The applicant shall also include a financial certification or disclosure statement(s) or both for clinical investigators as required by part 54 of this chapter. An application for a biologics license shall not be considered as filed until all pertinent information and data have been received by the Food and Drug Administration. The applicant shall also include either a claim for categorical exclusion under § 25.30 or § 25.31 of this chapter or an environmental assessment under § 25.40 of this chapter. The applicant, or the applicant's attorney, agent, or other authorized official shall sign the application. An application for any of the following specified categories of biological products subject to licensure shall be handled as set forth in paragraph (c) of this section:

(1) Therapeutic DNA plasmid products;

(2) Therapeutic synthetic peptide products of 40 or fewer amino acids;

(3) Monoclonal antibody products for in vivo use; and

(4) Therapeutic recombinant DNA-derived products.

(b) [Reserved]

(c)(1) To obtain marketing approval for a biological product subject to licensure which is a therapeutic DNA plasmid product, therapeutic synthetic peptide product of 40 or fewer amino acids, monoclonal antibody product for in vivo use, or therapeutic recombinant DNA-derived product, an applicant shall submit a biologics license application in accordance with paragraph (a) of this section except that the following sections in parts 600 through 680 of this chapter shall not be applicable to such products: §§ 600.10(b) and (c), 600.11, 600.12, 600.13, 610.53, and 610.62 of this chapter.

(2) To the extent that the requirements in this paragraph (c) conflict with other requirements in this subchapter, this paragraph (c) shall supersede other requirements.

(d) Approval of a biologics license application or issuance of a biologics license shall constitute a determination that the establishment(s) and the product meet applicable requirements to ensure the continued safety, purity, and potency of such products. Applicable requirements for the maintenance of establishments for the manufacture of a product subject to this section shall include but not be limited to the good manufacturing practice requirements set forth in parts 210, 211, 600, 606, and 820 of this chapter.

(e) Any establishment and product license for a biological product issued under section 351 of the Public Health Service Act (42 U.S.C. 201 *et seq.*) that has not been revoked or suspended as of December 20, 1999, shall constitute an approved biologics license application in effect under the same terms and conditions set forth in such product license and such portions of the establishment license relating to such product.

(f) *Withdrawal from sale of approved biological products.* A holder of a biologics license application (BLA) must report to FDA, in accordance with the requirements of §§ 207.61 and 207.65, the withdrawal from sale of an approved biological product. The information must be submitted to FDA within 30 working days of the biological product's withdrawal from sale. The following information must be submitted: The holder's name; product name; BLA number; the National Drug Code; and the date on which the product is expected to be

no longer in commercial distribution. The reason for the withdrawal of the biological product is requested but not required to be submitted.

(g) *Master files*—(1) *Biologics license applications under section 351 of the Public Health Service Act not permitted to incorporate by reference drug substance, drug substance intermediate, or drug product information contained in a master file.* Except as provided in paragraphs (g)(2) and (3) of this section, a biologics license application under section 351 of the Public Health Service Act may not incorporate by reference drug substance, drug substance intermediate, or drug product information contained in a master file, including a drug master file submitted under § 314.420 of this chapter, for the product, including for a biological product constituent part of a combination product.

(2) *Former approved applications deemed to be licenses for biological products pursuant to section 7002(e)(4) of the Biologics Price Competition and Innovation Act of 2009.* An application for a biological product that:

(i) Is a former approved application under section 505 of the Federal Food, Drug, and Cosmetic Act that, pursuant to section 7002(e)(4) of the Biologics Price Competition and Innovation Act of 2009, has been deemed to be a license for the biological product under section 351 of the Public Health Service Act; and

(ii) At the time it was so deemed, incorporated by reference drug substance, drug substance intermediate, and/or drug product information contained in a drug master file submitted under § 314.420 of this chapter, may continue to incorporate by reference the information contained in that drug master file. Amendments and supplements to such applications may also continue to incorporate by reference the information contained in that drug master file.

(3) *Non-biological product constituent parts of combination products regulated under biologics license applications under section 351 of the Public Health Service Act.* A biologics license application under section 351 of the Public Health Service Act may incorporate by reference drug substance, drug substance intermediate, and/or drug product information contained in a master file, including a drug master file submitted under § 314.420 of this chapter, for any non-biological product constituent part of a combination product.

(4) *Biologics license applications under section 351 of the Public Health Service Act permitted to incorporate by reference information contained in a master file that is not drug substance, drug substance intermediate, or drug product information.* Nothing in paragraph (g)(1) of this section limits or restricts a biologics license application under section 351 of the Public Health Service Act from incorporating by reference information contained in any master file, including a drug master file submitted under § 314.420 of this chapter, that is not drug substance, drug substance intermediate, or drug product information.

(5) *Investigational new drug applications.* Nothing in paragraph (g)(1) of this section limits or restricts an investigational new drug application for a product that would be subject to licensure under section 351 of the Public Health Service Act from incorporating by reference any information, including drug substance, drug substance intermediate, and drug product information, contained in a master file, including a drug master file submitted under § 314.420 of this chapter.

[64 FR 56450, Oct. 20, 1999, as amended at 70 FR 14983, Mar. 24, 2005; 80 FR 18092, Apr. 3, 2015; 80 FR 37974, July 2, 2015; 81 FR 60221, Aug. 31, 2016; 89 FR 9756, Feb. 12, 2024]

§ 601.3 Complete response letter to the applicant.

(a) *Complete response letter.* The Food and Drug Administration will send the biologics license applicant or supplement applicant a complete response letter if the agency determines that it will not approve the biologics license application or supplement in its present form.

(1) *Description of specific deficiencies.* A complete response letter will describe all of the deficiencies that the agency has identified in a biologics license application or supplement, except as stated in paragraph (a)(2) of this section.

(2) *Inadequate data.* If FDA determines, after a biologics license application or supplement is filed, that the