AUTHENTICATED
U.S. GOVERNMENT
INFORMATION
GPO

required by § 601.12, (4) the establishment or any location thereof, or the product for which the license has been issued, fails to conform to the applicable standards established in the license and in this chapter designed to ensure the continued safety, purity, and potency of the manufactured product, (5) the establishment or the manufacturing methods have been so changed as to require a new showing that the establishment or product meets the standards established in this chapter in order to protect the public health, or (6) the licensed product is not safe and effective for all of its intended uses or is misbranded with respect to any such use, he shall notify the licensee of his intention to revoke the license, setting forth the grounds for, and offering an opportunity for a hearing on, the proposed revocation. Except as provided in § 601.6 or in cases involving willfulness, the notification required in this paragraph shall provide a reasonable period for the licensee to demonstrate or achieve compliance with the requirements of this chapter, before proceedings will be instituted for the revocation of the license. If compliance is not demonstrated or achieved and the licensee does not waive the opportunity for a hearing, the Commissioner shall issue a notice of opportunity for hearing on the matter pursuant to § 12.21(b) of this chapter.

[42 FR 4718, Jan. 25, 1977, as amended at 42 FR 15676, Mar. 22, 1977; 42 FR 19143, Apr. 12, 1977; 49 FR 23833, June 8, 1984]

§ 601.6 Suspension of license.

(a) Whenever the Commissioner has reasonable grounds to believe that any of the grounds for revocation of a license exist and that by reason thereof there is a danger to health, he may notify the licensee that his license for the establishment or the product is suspended and require that the licensee (1) notify the selling agents and distributors to whom such product or products have been delivered of such suspension, and (2) furnish to the Director, Center for Biologics Evaluation and Research, complete records of such deliveries and notice of suspension.

(b) Upon suspension of a license, the Commissioner shall either (1) proceed pursuant to the provisions of § 601.5(b) to revoke the license, or (2) if the licensee agrees, hold revocation in abeyance pending resolution of the matters involved.

[42 FR 4718, Jan. 25, 1977 as amended at 49 FR 23833, June 8, 1984; 55 FR 11013, Mar. 26, 1990]

§ 601.7 Procedure for hearings.

(a) A notice of opportunity for hearing, notice of appearance and request for hearing, and grant or denial of hearing for a biological drug pursuant to this part, for which the exemption from the Federal Food, Drug, and Cosmetic Act in § 310.4 of this chapter has been revoked, shall be subject to the provisions of § 314.200 of this chapter except to the extent that the notice of opportunity for hearing on the matter issued pursuant to § 12.21(b) of this chapter specifically provides otherwise.

(b) Hearings pursuant to §§ 601.4 through 601.6 shall be governed by part 12 of this chapter.

(c) When a license has been suspended pursuant to § 601.6 and a hearing request has been granted, the hearing shall proceed on an expedited basis.

[42 FR 4718, Jan. 25, 1977, as amended at 42 FR 15676, Mar. 22, 1977; 42 FR 19143, Apr. 12, 1977]

§ 601.8 Publication of revocation.

Notice of revocation of a license, with statement of the cause therefor, shall be issued by the Commissioner and published in the FEDERAL REGISTER.

[42 FR 4718, Jan. 25, 1977]

§ 601.9 Licenses; reissuance.

(a) *Compliance with standards.* An establishment or product license, previously suspended or revoked, may be reissued or reinstated upon a showing of compliance with required standards and upon such inspection and examination as may be considered necessary by the Director, Center for Biologics Evaluation and Research.

(b) *Exclusion of noncomplying location.* An establishment or product license, excluding a location or locations that fail to comply with required standards, may be issued without further application and concurrently with the suspension or revocation of the license for

noncompliance at the excluded location or locations.

[42 FR 4718, Jan. 25, 1977, as amemded at 49 FR 23833, June 8, 1984; 55 FR 11013, Mar. 26, 1990]

Subpart B—Establishment Licensing

§ 601.10 Establishment licenses; issuance and conditions.

(a) *Inspection—compliance with standards.* An establishment license shall be issued only after inspection of the establishment and upon a determination that the establishment complies with the applicable standards prescribed in the regulations in this subchapter.

(b) *Availability of product; simultaneous request for and issuance of product license.* No establishment license shall be issued unless (1) a product intended for sale, barter or exchange or intended to be offered, sent, carried or brought for sale, barter or exchange is available for examination, (2) such product is available for inspection during all phases of manufacture and (3) a product license is requested and issued simultaneously with the establishment license.

(c) *One establishment license to cover all locations.* One establishment license shall be issued to cover all locations meeting the establishment standards.

§ 601.12 Changes to an approved application.

(a) *General.* As provided by this section, an applicant shall inform Food and Drug Administration (FDA) about each change in the product, production process, quality controls, equipment, facilities, responsible personnel, or labeling, established in the approved license application(s). Before distributing a product made using a change, an applicant shall demonstrate through appropriate validation and/or other clinical and/or non-clinical laboratory studies, the lack of adverse effect of the change on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product.

(b) *Changes requiring supplement submission and approval prior to distribution of the product made using the change (major changes).* (1) A supplement shall be submitted for any change in the product, production process, quality controls, equipment, facilities, or responsible personnel that has a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product.

(2) These changes include, but are not limited to:

(i) Changes in the qualitative or quantitative formulation or other specifications as provided in the approved application or in the regulations;

(ii) Changes requiring completion of an appropriate human study to demonstrate the equivalence of the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product;

(iii) Changes in the virus or adventitious agent removal or inactivation method(s);

(iv) Changes in the source material or cell line;

(v) Establishment of a new master cell bank or seed; and

(vi) Changes which may affect product sterility assurance, such as changes in product or component sterilization method(s), or an addition, deletion, or substitution of steps in an aseptic processing operation.

(3) The applicant must obtain approval of the supplement from FDA prior to distribution of the product made using the change. Except for submissions under paragraph (e) of this section, the following shall be contained in the supplement:

(i) A detailed description of the proposed change;

(ii) The product(s) involved;

(iii) The manufacturing site(s) or area(s) affected;

(iv) A description of the methods used and studies performed to evaluate the effect of the change on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product;

(v) The data derived from such studies;

(vi) Relevant validation protocols and data; and