

or "Investigational New Drug Application" was submitted to the Center for Drug Evaluation and Research on or before August 25, 1975 is terminated on August 20, 1976, unless an approvable notice was issued on or before August 20, 1976, in which case the exemption is terminated either upon the subsequent issuance of a nonapprovable notice for the new drug application or on November 20, 1976, whichever occurs first.

(ii) The exemption referred to in paragraph (a) of this section, as applied to any biologic containing any of the isotopes listed in paragraph (f)(1) of this section in the "chemical form" and intended for the uses stated, for which biologic an application for product license or "Investigational New Drug Application" was submitted to the Center for Biologics Evaluation and Research on or before August 25, 1975 is terminated on October 20, 1976, unless an approvable notice was issued on or before October 20, 1976, in which case the exemption is terminated either upon the subsequent issuance of a nonapprovable notice for the new drug application or on January 20, 1977, whichever occurs first.

(g) The exemption referred to in paragraph (a) of this section, as applied to any drug intended solely for investigational use as part of a research project, which use had been approved on or before July 25, 1975 in accordance with 10 CFR 35.11 (or equivalent regulation of an Agreement State) is terminated on February 20, 1976 if the manufacturer of such drug or the sponsor of the investigation of such drug submits on or before August 25, 1975 to the Food and Drug Administration, Bureau of Drugs, HFD-150, 5600 Fishers Lane, Rockville, MD 20857, the following information:

- (1) The research project title;
- (2) A brief description of the purpose of the project;
- (3) The name of the investigator responsible;
- (4) The name and license number of the institution holding the specific license under 10 CFR 35.11 (or equivalent regulation of an Agreement State);
- (5) The name and maximum amount per subject of the radionuclide used;
- (6) The number of subjects involved; and

(7) The date on which the administration of the radioactive drugs is expected to be completed.

(h) The exemption referred to in paragraph (a) of this section, as applied to any drug not referred to in paragraphs (d), (f), and (g) of this section, is terminated on August 26, 1975.

[39 FR 11680, Mar. 29, 1974, as amended at 40 FR 31307, July 25, 1975; 40 FR 44543, Sept. 29, 1975; 41 FR 35171, Aug. 20, 1976; 41 FR 42947, Sept. 29, 1976; 50 FR 8996, Mar. 6, 1985; 55 FR 11578, Mar. 29, 1990; 64 FR 56449, Oct. 20, 1999]

#### § 310.509 Parenteral drug products in plastic containers.

(a) Any parenteral drug product packaged in a plastic immediate container is not generally recognized as safe and effective, is a new drug within the meaning of section 201(p) of the act, and requires an approved new drug application as a condition for marketing. An "Investigational New Drug Application" set forth in part 312 of this chapter is required for clinical investigations designed to obtain evidence of safety and effectiveness.

(b) As used in this section, the term "large volume parenteral drug product" means a terminally sterilized aqueous drug product packaged in a single-dose container with a capacity of 100 milliliters or more and intended to be administered or used intravenously in a human.

(c) Until the results of compatibility studies are evaluated, a large volume parenteral drug product for intravenous use in humans that is packaged in a plastic immediate container on or after April 16, 1979, is misbranded unless its labeling contains a warning that includes the following information:

- (1) A statement that additives may be incompatible.
- (2) A statement that, if additive drugs are introduced into the parenteral system, aseptic techniques should be used and the solution should be thoroughly mixed.
- (3) A statement that a solution containing an additive drug should not be stored.

(d) This section does not apply to a biological product licensed under the

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Public Health Service Act of July 1, 1944 (42 U.S.C. 201).

[62 FR 12084, Mar. 14, 1997]

### § 310.515 Patient package inserts for estrogens.

(a) *Requirement for a patient package insert.* FDA concludes that the safe and effective use of drug products containing estrogens requires that patients be fully informed of the benefits and risks involved in the use of these drugs. Accordingly, except as provided in paragraph (e) of this section, each estrogen drug product restricted to prescription distribution, including products containing estrogens in fixed combinations with other drugs, shall be dispensed to patients with a patient package insert containing information concerning the drug's benefits and risks. An estrogen drug product that does not comply with the requirements of this section is misbranded under section 502(a) of the Federal Food, Drug, and Cosmetic Act.

(b) *Distribution requirements.* (1) For estrogen drug products, the manufacturer and distributor shall provide a patient package insert in or with each package of the drug product that the manufacturer or distributor intends to be dispensed to a patient.

(2) In the case of estrogen drug products in bulk packages intended for multiple dispensing, and in the case of injectables in multiple-dose vials, a sufficient number of patient labeling pieces shall be included in or with each package to assure that one piece can be included with each package or dose dispensed or administered to every patient. Each bulk package shall be labeled with instructions to the dispenser to include one patient labeling piece with each package dispensed or, in the case of injectables, with each dose administered to the patient. This section does not preclude the manufacturer or labeler from distributing additional patient labeling pieces to the dispenser.

(3) Patient package inserts for estrogens dispensed in acute-care hospitals or long-term care facilities will be considered to have been provided in accordance with this section if provided to the patient before administration of the first estrogen and every 30 days

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thereafter, as long as the therapy continues.

(c) *Patient package insert contents.* A patient package insert for an estrogen drug product is required to contain the following information:

(1) The name of the drug.

(2) The name and place of business of the manufacturer, packer, or distributor.

(3) A statement regarding the benefits and proper uses of estrogens.

(4) The contraindications to use, *i.e.*, when estrogens should not be used.

(5) A description of the most serious risks associated with the use of estrogens.

(6) A brief summary of other side effects of estrogens.

(7) Instructions on how a patient may reduce the risks of estrogen use.

(8) The date, identified as such, of the most recent revision of the patient package insert.

(d) *Guidance language.* The Food and Drug Administration issues informal labeling guidance texts under § 10.90(b)(9) of this chapter to provide assistance in meeting the requirements of paragraph (c) of this section. Requests for a copy of the guidance text should be directed to the Center for Drug Evaluation and Research, Division of Reproductive and Urologic Products, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993–0002.

(e) *Exemptions.* This section does not apply to estrogen-progestogen oral contraceptives. Labeling requirements for these products are set forth in § 310.501.

(f) *Requirement to supplement approved application.* Holders of approved applications for estrogen drug products that are subject to the requirements of this section must submit supplements under § 314.70(c) of this chapter to provide for the labeling required by paragraph (a) of this section. Such labeling may be put into use without advance approval by the Food and Drug Administration.

[55 FR 18723, May 4, 1990, as amended at 74 FR 13113, Mar. 26, 2009]