

bioavailability study in which the sample from which the reserve sample was obtained was used.

(f) Authorized FDA personnel will ordinarily collect reserve samples directly from the applicant or contract research organization at the storage site during a preapproval inspection. If authorized FDA personnel are unable to collect samples, FDA may require the applicant or contract research organization to submit the reserve samples to the place identified in the agency's request. If FDA has not collected or requested delivery of a reserve sample, or if FDA has not collected or requested delivery of any portion of a reserve sample, the applicant or contract research organization shall retain the sample or remaining sample for the 5-year period specified in paragraph (e) of this section.

(g) Upon release of the reserve samples to FDA, the applicant or contract research organization shall provide a written assurance that, to the best knowledge and belief of the individual executing the assurance, the reserve samples came from the same samples as used in the specific bioavailability or bioequivalence study identified by the agency. The assurance shall be executed by an individual authorized to act for the applicant or contract research organization in releasing the reserve samples to FDA.

(h) A contract research organization may contract with an appropriate, independent third party to provide storage of reserve samples provided that the sponsor of the study has been notified in writing of the name and address of the facility at which the reserve samples will be stored.

(i) If a contract research organization conducting a bioavailability or bioequivalence study that requires reserve sample retention under this section or § 320.63 goes out of business, it shall transfer its reserve samples to an appropriate, independent third party, and shall notify in writing the sponsor of the study of the transfer and provide the study sponsor with the name and address of the facility to which the reserve samples have been transferred.

[58 FR 25927, Apr. 28, 1993, as amended at 64 FR 402, Jan. 5, 1999]

### § 320.63 Retention of bioequivalence samples.

The applicant of an abbreviated application or a supplemental application submitted under section 505 of the Federal Food, Drug, and Cosmetic Act, or, if bioequivalence testing was performed under contract, the contract research organization shall retain reserve samples of any test article and reference standard used in conducting an in vivo or in vitro bioequivalence study required for approval of the abbreviated application or supplemental application. The applicant or contract research organization shall retain the reserve samples in accordance with, and for the period specified in, § 320.38 and shall release the reserve samples to FDA upon request in accordance with § 320.38.

[58 FR 25928, Apr. 28, 1993, as amended at 64 FR 402, Jan. 5, 1999]

## PART 328—OVER-THE-COUNTER DRUG PRODUCTS INTENDED FOR ORAL INGESTION THAT CONTAIN ALCOHOL

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AUTHORITY: Secs. 201, 301, 501, 502, 503, 505, 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 331, 351, 352, 353, 355, 371).

SOURCE: 60 FR 13595, Mar. 13, 1995, unless otherwise noted.

EDITORIAL NOTE: Nomenclature changes to part 328 appear at 69 FR 13717, Mar. 24, 2004.

### Subpart A—General Provisions

#### § 328.1 Scope.

Reference in this part to regulatory sections of the Code of Federal Regulations are to chapter I of title 21 unless otherwise noted.

## § 328.3

### § 328.3 Definitions.

As used in this part:

(a) *Alcohol* means the substance known as ethanol, ethyl alcohol, or Alcohol, USP.

(b) *Inactive ingredient* means any component of a product other than an active ingredient as defined in § 210.3(b)(7) of this chapter.

## Subpart B—Ingredients

### § 328.10 Alcohol.

(a) Any over-the-counter (OTC) drug product intended for oral ingestion shall not contain alcohol as an inactive ingredient in concentrations that exceed those established in this part, unless a specific exemption, as provided in paragraph (e) or (f) of this section, has been approved.

(b) For any OTC drug product intended for oral ingestion and labeled for use by adults and children 12 years of age and over, the amount of alcohol in the product shall not exceed 10 percent.

(c) For any OTC drug product intended for oral ingestion and labeled for use by children 6 to under 12 years of age, the amount of alcohol in the product shall not exceed 5 percent.

(d) For any OTC drug product intended for oral ingestion and labeled for use by children under 6 years of age, the amount of alcohol in the product shall not exceed 0.5 percent.

(e) The Food and Drug Administration will grant an exemption from paragraphs (b), (c), and (d) of this section where appropriate, upon petition under the provisions of § 10.30 of this chapter. Appropriate cause, such as a specific solubility or manufacturing problem, must be adequately documented in the petition. Decisions with respect to requests for exemption shall be maintained in a permanent file for public review by the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

(f) Ipecac syrup is exempt from the provisions of paragraph (d) of this section.

(g) The following drugs are temporarily exempt from the provisions of

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paragraphs (b), (c), and (d) of this section:

- (1) Aromatic Cascara Fluidextract.
- (2) Cascara Sagrada Fluidextract.
- (3) Orally ingested homeopathic drug products.

[60 FR 13595, Mar. 13, 1995, as amended at 61 FR 58630, Nov. 18, 1996; 68 FR 24879, May 9, 2003]

## Subpart C—Labeling

### § 328.50 Principal display panel of all OTC drug products intended for oral ingestion that contain alcohol.

(a) The amount (percentage) of alcohol present in a product shall be stated in terms of percent volume of absolute alcohol at 60 °F (15.56 °C) in accordance with § 201.10(d)(2) of this chapter.

(b) A statement expressing the amount (percentage) of alcohol present in a product shall appear prominently and conspicuously on the “principal display panel,” as defined in § 201.60 of this chapter. For products whose principal display panel is on the immediate container label and that are not marketed in another retail package (e.g., an outer box), the statement of the percentage of alcohol present in the product shall appear prominently and conspicuously on the “principal display panel” of the immediate container label.

(c) For products whose principal display panel is on the retail package and the retail package is not the immediate container, the statement of the percentage of alcohol present in the product shall also appear on the immediate container label; it may appear anywhere on that label in accord with section 502(e) of the Federal Food, Drug, and Cosmetic Act.

(d) The statement expressing the amount (percentage) of alcohol present in the product shall be in a size reasonably related to the most prominent printed matter on the panel or label on which it appears, and shall be in lines generally parallel to the base on which the package rests as it is designed to be displayed.

(e) For a product to state in its labeling that it is “alcohol free,” it must contain no alcohol (0 percent).

(f) For any OTC drug product intended for oral ingestion containing

over 5 percent alcohol and labeled for use by adults and children 12 years of age and over, the labeling shall contain the following statement in the directions section: "Consult a physician for use in children under 12 years of age."

(g) For any OTC drug product intended for oral ingestion containing over 0.5 percent alcohol and labeled for use by children ages 6 to under 12 years of age, the labeling shall contain the following statement in the directions section: "Consult a physician for use in children under 6 years of age."

(h) When the direction regarding age in paragraph (e) or (f) of this section differs from an age-limiting direction contained in any OTC drug monograph in this chapter, the direction containing the more stringent age limitation shall be used.

**PART 329—NONPRESCRIPTION HUMAN DRUG PRODUCTS SUBJECT TO SECTION 760 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT**

AUTHORITY: 21 U.S.C. 321, 331, 351, 352, 353, 355, 371, 379aa.

SOURCE: 79 FR 33089, June 10, 2014, unless otherwise noted.

**§ 329.100 Postmarketing reporting of adverse drug events under section 760 of the Federal Food, Drug, and Cosmetic Act.**

(a) *Reporting requirements.* Reports of serious adverse events required by section 760 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) must include the information specified in this section, as applicable. Except as provided in paragraph (c)(2) of this section, these reports must be submitted to the Agency in electronic format as described in paragraph (c)(1) of this section.

(b) *Contents of reports.* For purposes of reporting serious adverse events under section 760 of the FD&C Act, an individual case safety report (ICSR) constitutes the MedWatch form required to be submitted by section 760(d) of the FD&C Act. ICSRs include the following information:

(1) *Patient information.*

(i) Patient identification code;

(ii) Patient age at the time of adverse drug experience, or date of birth;

(iii) Patient gender; and

(iv) Patient weight.

(2) *Adverse event.*

(i) Outcome attributed to adverse drug event;

(ii) Date of adverse drug event;

(iii) Date of ICSR submission;

(iv) Description of adverse drug event (including a concise medical narrative);

(v) Adverse drug event term(s);

(vi) Description of relevant tests, including dates and laboratory data; and

(vii) Other relevant patient history, including preexisting medical conditions.

(3) *Suspect medical product(s).*

(i) Name;

(ii) Dose, frequency, and route of administration used;

(iii) Therapy dates;

(iv) Diagnosis for use (indication);

(v) Whether the product is a combination product as defined in §3.2(e) of this chapter;

(vi) Whether the product is a prescription or nonprescription product;

(vii) Whether adverse drug event abated after drug use stopped or dose reduced;

(viii) Whether adverse drug event reappeared after reintroduction of drug;

(ix) Lot number;

(x) Expiration date;

(xi) National Drug Code (NDC) number; and

(xii) Concomitant medical products and therapy dates.

(4) *Initial reporter information.*

(i) Name, address, and telephone number;

(ii) Whether the initial reporter is a health care professional; and

(iii) Occupation, if a health care professional.

(5) *Responsible person (as defined in section 760(b) of the FD&C Act) information.*

(i) Name and contact office address;

(ii) Telephone number;

(iii) Report source, such as spontaneous;

(iv) Date the report was received by responsible person;

(v) Whether the ICSR is a 15-day report;

(vi) Whether the ICSR is an initial report or followup report; and