

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

Subpart A—General Provisions

Sec.

328.1 Scope.

328.3 Definitions.

Subpart B—Ingredients

328.10 Alcohol.

Subpart C—Labeling

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

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 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

Subpart C—Labeling

§ 328.10 Alcohol.

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

(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) 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.

(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 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.

(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) 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.

(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) 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.

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

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

(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) The following drugs are temporarily exempt from the provisions of paragraphs (b), (c), and (d) of this section:

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

(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

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

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 330—OVER-THE-COUNTER (OTC) HUMAN DRUGS WHICH ARE GENERALLY RECOGNIZED AS SAFE AND EFFECTIVE AND NOT MISBRANDED

Subpart A—General Provisions

Sec.

330.1 General conditions for general recognition as safe, effective and not misbranded.

330.2 Pregnancy-nursing warning.

330.3 Imprinting of solid oral dosage form drug products.

330.5 Drug categories.

Subpart B—Administrative Procedures

330.10 Procedures for classifying OTC drugs as generally recognized as safe and effective and not misbranded, and for establishing monographs.

330.11 NDA deviations from applicable monograph.

330.12 Status of over-the-counter (OTC) drugs previously reviewed under the Drug Efficacy Study (DES).

330.13 Conditions for marketing ingredients recommended for over-the-counter (OTC) use under the OTC drug review.

330.14 Additional criteria and procedures for classifying OTC drugs as generally recognized as safe and effective and not misbranded.

AUTHORITY: 21 U.S.C. 321, 351, 352, 353, 355, 360, 371.

SOURCE: 39 FR 11741, Mar. 29, 1974, unless otherwise noted.

EDITORIAL NOTE: Nomenclature changes to part 330 appear at 69 FR 13717, Mar. 24, 2004.

Subpart A—General Provisions

§ 330.1 General conditions for general recognition as safe, effective and not misbranded.

An over-the-counter (OTC) drug listed in this subchapter is generally rec-

ognized as safe and effective and is not misbranded if it meets each of the conditions contained in this part and each of the conditions contained in any applicable monograph. Any product which fails to conform to each of the conditions contained in this part and in an applicable monograph is liable to regulatory action.

(a) The product is manufactured in compliance with current good manufacturing practices, as established by parts 210 and 211 of this chapter.

(b) The establishment(s) in which the drug product is manufactured is registered, and the drug product is listed, in compliance with part 207 of this chapter. It is requested but not required that the number assigned to the product pursuant to part 207 of this chapter appear on all drug labels and in all drug labeling. If this number is used, it shall be placed in the manner set forth in part 207 of this chapter.

(c)(1) The product is labeled in compliance with chapter V of the Federal Food, Drug, and Cosmetic Act (the act) and subchapter C *et seq.* of this chapter, including the format and content requirements in §201.66 of this chapter. An OTC drug product that is not in compliance with chapter V and subchapter C, including §201.66 of this chapter, is subject to regulatory action. For purposes of §201.61(b) of this chapter, the statement of identity of the product shall be the term or phrase used in the applicable OTC drug monograph established in this part.

(2) The “Uses” section of the label and labeling of the product shall contain the labeling describing the “Indications” that have been established in an applicable OTC drug monograph or alternative truthful and nonmisleading statements describing only those indications for use that have been established in an applicable monograph, subject to the provisions of section 502 of the act relating to misbranding and the prohibition in section 301(d) of the act against the introduction or delivery for introduction into interstate commerce of unapproved new drugs in violation of section 505(a) of the act. Any other labeling under this subchapter and subchapter C *et seq.* of this chapter shall be stated in the exact language where exact language has been established