DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 328

[Docket No. 93N–0107]

Over-the-Counter Drug Products Intended for Oral Ingestion that Contain Alcohol

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule establishing a maximum concentration limit for alcohol (ethyl alcohol) as an inactive ingredient in over-the-counter (OTC) drug products intended for oral ingestion (0.5 percent alcohol for children under 6 years of age, 5 percent alcohol for children 6 to under 12 years of age, and 10 percent alcohol for anyone 12 years of age and over). This final rule also requires that the alcohol content be stated prominently and conspicuously on the principal display (front) panel of product labeling. FDA is issuing this final rule after considering recommendations from its Nonprescription Drugs Advisory Committee (NDAC) and public comments on the agency's notice of proposed rulemaking. This final rule defers action on alcohol limits for Aromatic Cascara Fluidextract, Cascara Sagrada Fluidextract, and orally ingested OTC homeopathic drug products.

EFFECTIVE DATE: March 13, 1996.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drug Evaluation and Research (HFD–810), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–594–5000.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of October 21, 1993 (58 FR 54466), the agency proposed maximum concentration limits for alcohol as an inactive ingredient in OTC drug products intended for oral ingestion. The proposed limits were 0.5 percent alcohol for children under 6 years of age, 5 percent alcohol for children 6 to under 12 years of age, and 10 percent alcohol for anyone 12 years of age and over. In addition, the agency proposed that the alcohol content be stated prominently and conspicuously on the principal display (front) panel of product labeling, and that the labeling term ''alcohol-free'' mean that the product contains no alcohol at all. These proposals were based on NDAC's recommendations.

In response to the proposal, seven drug manufacturers, four professional organizations, four drug manufacturers associations, and two consumers submitted comments. Copies of the comments are on public display in the Dockets Management Branch (HFA–305), Food and Drug Administration, rm. 1–23, 12420 Parklawn Dr., Rockville, MD 20857.

I. The Agency's Conclusions on the Comments

A. General Comments

1. Several comments expressed their support for the alcohol content limitations proposed by the agency and placement of the alcohol content on the front (principal) display panel. The comments stated that prominent and conspicuous labeling will enhance and guide the public in making an informed decision when purchasing products.

2. Two comments urged FDA and industry to find alternatives to alcohol so that eventually alcohol can be eliminated from OTC drug products entirely. One comment, from a manufacturer of nonalcoholic OTC drug products, suggested that the agency codify its policy of encouragement of the lowest amount of alcohol necessary for pharmaceutical purposes. The comment stated that this could be done by amending proposed § 328.10 to include new paragraph (f) as follows:

(f) Any manufacturer of OTC drug products shall use, within reasonable time of it becoming known, any formulary technique or technology commercially available at adoption of this rule or which may later become available and would optimally reduce or eliminate the use of alcohol in its OTC product(s).

The agency appreciates the comments' concerns and strongly encourages the further development of safe alternatives to alcohol. However, the agency believes that it is unnecessary to codify its policy of ''encouragement,'' as suggested by one comment. The agency's statements in the preamble to the proposal and the agency's action in implementing alcohol concentration limits adequately reflect the agency's policy to reduce the amount of alcohol in OTC drug products.

3. One comment requested that FDA adopt a timetable for implementation of the new alcohol content limitations for orally ingested OTC drug products that is consistent with the timetable in the voluntary program proposed by the Nonprescription Drugs Manufacturers Association (NDMA). That program calls for NDMA member companies with affected products to implement the new limitations ''as soon as practicable.'' The goal for reformulating and labeling the 5- and 10-percent alcohol limitations was November 1993. The goal for reformulating and labeling of alcohol-free OTC drug products was December 1994. Both dates were for factory shipment of reformulated products.

The agency stated in its proposed rule (58 FR 54466) that the final rule would become effective 12 months after the date of its publication in the **Federal Register**. Thus, the effective date for implementing this final rule will go beyond the December 1994 date proposed by NDMA to complete the implementation of its voluntary program and should present no problems timewise to NDMA member companies.

4. One comment contended that the alcohol content regulation should pertain solely to orally ingested products covered by OTC drug monographs. The comment stated that OTC drug monographs represent a menu of ingredients that represent an essentially known set of products from a formulation standpoint, while OTC drug products under new drug applications (NDA's) usually represent novel OTC formulations that may require special considerations regarding product specifications. The comment added that formulatory flexibility is especially needed in the future for prescription-to-OTC switch products under NDA's.

The agency disagrees with the comment. The intent of the regulation is to limit the alcohol content of all OTC drug products intended for oral ingestion, regardless whether marketed under an OTC drug monograph(s) or an NDA (which also includes abbreviated applications). The regulation provides an exemption procedure in § 328.10(e). Appropriate cause, such as a specific solubility or manufacturing problem, must be adequately documented. This procedure applies equally to products marketed under an OTC drug monograph(s) or an NDA. Therefore, the agency finds no basis to limit the regulation solely to products covered by OTC drug monographs.

5. One comment asserted that the proposed rule should be withdrawn because there are no data to support a 10-percent alcohol limit for orally ingested OTC drug products intended for adults. The comment contended that the 10-percent maximum alcohol concentration for adults was based solely on scientific opinion, but without scientific data to support the opinion. The comment argued that requiring

manufacturers to apply for an exemption to exceed the 10-percent alcohol content limit is unwarranted because the agency has not shown that such products are dangerous.

The agency disagrees with the comment. A number of safety issues related to higher alcohol concentrations were discussed at the NDAC meeting held on December 17, 1992. NDAC discussed development of lactic acidosis (with hypoglycemia occurring in some people) in acute alcohol intoxication, sensitivity and tolerance to alcohol, cutaneous vasodilation, withdrawal syndrome, fetal alcohol syndrome, interaction with drugs, etc. (See 58 FR 54466 at 54467 to 54468.) NDAC considered that alcohol displays zero order pharmacokinetics once a threshold concentration is exceeded. This means that blood alcohol concentrations are not proportional to the amount ingested. Thus, a small increase in the amount ingested may lead to a large increase in the blood alcohol concentration. It therefore is much easier to attain intoxicating blood levels of alcohol, because less alcohol needs to be ingested to do so.

The agency believes that there are sufficient scientific data to support the 10-percent alcohol limit for orally ingested OTC drug products intended for adults and that the petition procedure in § 328.10(e) is appropriate if there is a need to request an exemption.

6. One comment claimed that requiring child-resistant (CR) packaging would be more helpful in preventing accidental overdose in children than the alcohol content limitations proposed by the agency. The comment noted that the Consumer Product Safety Commission (CPSC) is currently considering development of a regulation to require CR packaging for mouthwashes containing greater than five percent alcohol. The comment mentioned that in response to the continuing problem of tampering with OTC drug products formulated as two-piece hard gelatin capsules, FDA had not proposed to simply ban gelatin capsules but rather ''balanced the value of the hard capsule dosage form to consumers against its continued vulnerability to malicious tampering'' and proposed to strengthen its tamper-resistant packaging regulation (59 FR 2542 at 2543, January 18, 1994).

The agency believes that CR packaging could play a role in preventing toxic effects in infants and young children from accidental ingestion of alcohol-containing OTC drug products. However, CR packaging alone would not prevent adolescents and adults from intentionally ingesting OTC drug products for their alcohol content or prevent young children and adolescents from ingesting undesirable levels of alcohol from normal doses of alcohol-containing OTC drug products. Because prevention of accidental overdose in children is not the primary purpose of this regulation, the agency is finalizing the regulation as proposed.

The agency discussed the issue of CR packaging in the OTC cough-cold combinations tentative final monograph (53 FR 30522 at 30527, August 12, 1988), and stated that the authority to require CR packaging rests with the CPSC under the Poison Prevention Packaging Act of 1970. FDA is aware that the CPSC has published a proposed rule (59 FR 24386, May 11, 1994) to require CR packaging for mouthwash products containing 3 grams (g) or more of alcohol. FDA is not aware of any CPSC consideration of CR packaging for alcohol-containing OTC drug products intended for oral ingestion.

7. One comment questioned why small amounts of alcohol ingested in OTC drug products are considered harmful when one to two ounces (oz) of alcohol per day are recommended for cardiovascular health in adults.

The agency acknowledges that small amounts of alcohol are not harmful for most adults. However, for some people even small amounts of alcohol could be harmful (see section I.A., comments 5 and 6). Those individuals will avoid alcoholic beverages but may not avoid OTC drug products because of unawareness of their alcohol content. The agency concludes that the potential benefit alcohol may have for cardiovascular health in some adults does not justify the unnecessary use of alcohol in OTC drug products, when this use may be harmful to some individuals.

8. One comment contended that eliminating alcohol from products intended for use by children and younger adolescents will not entirely address the problem posed by adolescents who purchase OTC drug products intended for use by adults in order to obtain psychoactive effects from the alcohol.

The agency acknowledges that the final regulation will not entirely eliminate the potential for adults and adolescents intentionally to misuse OTC drug products for their alcohol content. The prevention of intentional misuse, however, is not the primary consideration of this regulation. However, by reducing the amount of alcohol that can be consumed from OTC drug products, the agency believes that this regulation will discourage and reduce intentional misuse.

9. One comment requested that the agency have NDAC review the safety of synthetic alcohols (glycols) as a phase II followup to its initial ''alcohol'' work.

The agency notes that the comment offered no data or reasons to support its request. The agency is not aware of any current safety problems surrounding the use of glycols as inactive ingredients in OTC drug products that would warrant review at this time.

B. Comments on Labeling of OTC Drug Products Intended for Oral Ingestion that Contain Alcohol

10. Two comments objected to the requirement in proposed § 328.50(b) that the product's alcohol content appear on the principal display panel (PDP). The comments indicated that the PDP is for the purpose of product recognition and was not designed to carry all important information about safe product use, contending that the product information panel (PIP) was intended to provide this information. The comments stated that section 502(e) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 352(e)) allows the alcohol content to appear anywhere on the OTC label. The comments mentioned that it has been industry practice to place the alcohol content in the PIP under the inactive ingredients section. The comments indicated that when consumers question product content, they logically turn to the ingredient listing on the PIP. The comments added that alcohol content information on the PDP would overemphasize and detract from the PIP. One comment argued that including an alcohol content statement would inevitably decrease the ''conspicuousness'' and prominence of other language currently required on the PDP. The other comment argued that it is important to use the PDP for its specialized marketing purposes (product recognition, e.g., product name, statement of identity, and net contents) and to use the PIP for consistent consumer usage of OTC drug labeling (e.g., ingredients, warnings, and directions) for all the various OTC drug categories. The comment added that a low alcohol content is not of any greater importance than other warnings currently required on OTC drug products intended for oral ingestion. The comment mentioned that consumers with a personal interest in the product's alcohol content will be self-motivated to read the PIP for the disclosed alcohol content. The comments noted that a number of other related important warnings (e.g., the aspartame warning for phenylketonurics on food products, the sodium content

warnings, and the FD&C Yellow No. 5 warnings in 21 CFR 201.20 for certain drugs) are not required to appear on the PDP, but may appear on the PIP.

One comment also stated that there is no demonstrable evidence of a serious public health hazard resulting from the presence of alcohol in OTC drug products. The comment argued that the use of the PDP to disclose alcohol content would create, by regulation, a negative perception of alcohol, which is unwarranted scientifically. The comment concluded that no data are available to suggest that the current labeling regulations are ineffective in informing consumers who want to know the alcohol content of OTC drug products.

The agency disagrees with the comments. While no specific data are available to demonstrate consumer confusion, the agency believes consumers need to be able to readily determine the alcohol content of OTC drug products at the time of purchase. The agency is aware that consumers do not necessarily read all labeling at the time of purchase. Prominent and conspicuous labeling of the alcohol content on the PDP will help consumers to make an informed decision at the time of purchase. This information is extremely important for consumers who wish to avoid or limit alcohol ingestion, such as a recovering alcoholic or a parent of a young child. The agency acknowledges that the act allows the alcohol content of a product to appear anywhere on the OTC label. However, the agency believes that the new alcohol labeling requirements should prove more effective in bringing this information to consumers' attention. The agency concludes that a few words describing the alcohol content (e.g., ''contains 5% alcohol,'' ''5% alcohol'') on the PDP would not significantly decrease label readability or alter the prominence of additional information currently required on the PDP. At this time, many manufacturers already voluntarily include related labeling to inform consumers that a product is ''alcohol free.'' To facilitate product comparison and to better provide consumers with information needed to make an informed decision, the agency is requiring a product's alcohol content to appear on the PDP. The agency is not aware of any significant safety problems with other inactive ingredients in OTC drug products that would warrant information about the ingredients on the PDP.

11. One comment expressed support for the agency's proposal that allows use of the term ''alcohol free'' only on those OTC drug products that contain no alcohol. Two comments objected to the proposal in § 328.50(e) that the term ''alcohol free'' mean zero percent alcohol. The comments requested that a de minimus level of alcohol be allowed in OTC drug products in order to permit some variability in the sensitivity of the methods of analysis and detection, especially due to the presence of alcohol moieties from natural flavors that are often used in OTC drug products. One comment argued that, due to the practicalities of pharmaceutical formulation, a de minimus level of 0.5 percent alcohol being labeled as ''alcohol free'' would allow manufacturers to use available alcohol-containing flavors in OTC drug formulations to provide essentially ''alcohol-free'' palatable formulations to consumers who want to avoid alcohol. The comment indicated that the terms ''sugar free'' (≤ 0.5 g), ''sodium free'' (≤ 5 mg), and ''fat free'' (≤ 0.5 g), may be applied to dietary supplements and foods (21 CFR 101.60(c)(1), 101.61(b)(1), and 101.62(b)(1)). The comment contended that this precedent acknowledges that a total absence of these components from certain foods is unlikely and difficult to achieve from the standpoint of product preparation. The comment concluded that this approach should carry over to an alcohol-free claim for OTC drug products.

The agency disagrees with the comments and believes that the term ''alcohol free'' should mean no (0 percent) alcohol in a product. The agency acknowledges that the total elimination of certain food components (fat, sugar, sodium) from foods is unlikely and difficult to achieve. Small amounts of these components, when present in foods, are dietarily insignificant. However, the agency believes that these circumstances do not apply to alcohol in OTC drug products.

Restricting use of the term ''alcohol free'' to products that contain no (0 percent) alcohol within the limits of current technology (Ref. 1) in no way limits manufacturers' ability to produce low alcohol OTC drug products. However, it does provide important and truthful labeling to consumers who may be interested in total avoidance of alcohol for personal, religious, or medical reasons. Consumers who want to purchase a product with no alcohol should be assured that the product does, in fact, contain no alcohol. Individuals taking an alcohol-deterrent medication, such as disulfiram, could suffer untoward reactions from ingesting a drug product labeled as ''alcohol free'' when it actually contains a small amount of alcohol (even up to 0.5 percent). Alcohol free products can be achieved, because a significant number of OTC drug products have already been reformulated with no alcohol. Therefore, the agency is finalizing § 328.50(e) as proposed.

The agency will use a gas-liquid chromatographic method (Ref. 1) to analyze products for their alcohol content. A copy of this method has been placed in the Dockets Management Branch (address above). The agency invites comments on this test method.

Reference

(1) Santos, J., ''Limit of Alcohol Test,'' draft of unpublished procedure, in OTC Vol. 260002, Docket No. 93N–0107, Dockets Management Branch.

12. One comment requested that the agency phase in the labeling requirements as they apply to homeopathic drug products over a period of 3 years. The comment contended that changing the labels on such a large number of preparations would require tremendous effort and expense. The comment added that this relabeling could not reasonably be achieved within the proposed 12-month period. Another comment complained that the agency is allowing manufacturers only 1 year to reformulate their products when it is impossible to achieve and prove a stable product formula in less than 3 years. The comment added that there may be no studies on the safety of increasing the amounts of alternative preservatives, while alcohol has a long history of safety.

The agency disagrees with the comments and finds no basis to grant a 3-year phase in period for this regulation. The comments offered no documentation to support that 3 years is necessary for product reformulation or relabeling. The agency feels that 1 year from the date of the final rule is sufficient for manufacturers to reformulate and relabel their products. One year has been the standard time provided for reformulation and relabeling throughout most of the OTC drug review. This timeframe has proven satisfactory for the vast majority of reformulations and relabelings that have resulted from the OTC drug review. Relabeling needed for homeopathic drug products to label the alcohol content on the principal display panel can be accomplished by the use of ''stick-on'' labels, if necessary.

The agency recognizes that manufacturers have already had 1 year since the proposal was published to conduct stability studies on products that will need to be reformulated. They will have 1 more year to complete these

studies before this final rule becomes effective. Further, manufacturers may request an extension for either relabeling or reformulating their products provided that they can justify and document their need.

C. Comments on Specific OTC Drug Products Containing Alcohol

13. One comment questioned whether the proposed regulations are intended to apply to homeopathic drug products. The comment noted that the preamble of the proposed rule stated that ''these regulations would apply to OTC drug products regulated under the monograph system (21 CFR parts 330 to 358), and those approved under new drug applications'' (58 FR 54466 at 54469). Referring to Compliance Policy Guide 7132.15 (homeopathic drugs) (Ref. 1) and the **Federal Register** announcement excluding OTC homeopathic drug products from the OTC drug review (37 FR 9464 at 9466, May 11, 1972), the comment mentioned that homeopathic drug products are not regulated under OTC drug monographs, nor are they subject to NDAs. The comment requested the agency to clarify this ambiguity.

The discussion in the preamble of the proposed rule about products regulated under the monograph system and NDA's was an illustrative example following a general statement that alcohol limitations and related labeling requirements apply to all OTC drug products intended for oral ingestion. It was the agency's intent that the proposed regulation apply to all drugs sold without a prescription. While homeopathic drugs are neither regulated under the monograph system nor subject to NDA's, they are still regulated as drugs under the act. The safety considerations surrounding alcohol apply equally to all OTC drug products. Accordingly, homeopathic drug products are subject to the final regulation and must meet all of the labeling requirements in § 328.50. However, because the regulation may conflict with alcohol content specifications set forth in the Homeopathic Pharmacopeia of the United States (see section I.C., comment 15), the agency is temporarily exempting orally ingested homeopathic drug products from the alcohol percentage limitations in § 328.10(b), (c), and (d) until this issue is resolved.

Reference

(1) FDA, Compliance Policy Guide 7132.15, May 31, 1988, copy in OTC Vol. 260002, Docket No. 93N–0107, Dockets Management Branch.

14. Two comments stated that the proposed regulation conflicts with the alcohol content specifications set forth in the Homeopathic Pharmacopoeia of the United States. Several comments argued that for solubility, stability, and preservative purposes, there is no substitute for alcohol in homeopathic drug products. Three of the comments added that alcohol is also essential in aiding the absorption of homeopathic medicines. The comments stated that ''if dilutions containing preservatives other than alcohol are used by a process of alternate serial dilution and dynaminization to prepare higher potencies, for example using a 3X formula to make a 6X, the preservatives would be potentized as well as the remedy in the homeopathic manner.'' The comments added that the physiological activity of homeopathically potentized preservatives is unknown and unpredictable, and no data exist to assist the homeopathic community in predicting the therapeutic effect on the user. Two comments mentioned that chemical preservatives have been identified increasingly as a source of undesired side effects, including allergies. One comment stated that the proposed alcohol restrictions would mean giving up all of the pharmaceutical, technical, and medical experience for homeopathic drug products. Another comment claimed that a therapeutic re-evaluation of homeopathic remedies would be necessary. Several comments claimed that alcohol in homeopathic drug products does not pose a risk to adults or children because of the small volume of alcohol present in a standard homeopathic drug dose (standard adult dose is generally 10 drops, 5 drops for children, approximately .25 to .5 mL) and the small package volume of alcohol containing homeopathic drug products (usually ≤ 4 oz). One comment stated that because the proposed alcohol content labeling focuses on percent alcohol content rather than total alcohol content per dose, consumers will avoid homeopathic drug products on the mistaken assumption that a high percent alcohol content reflects a high level of alcohol intake. Several comments asserted that the new regulation would have a significant ''negative'' economic impact on the homeopathic industry. The comments stated that a full-line homeopathic drug manufacturer makes dosage forms using over 1,000 active ingredients, and to reformulate, test, repackage, and relabel all homeopathic drug products would be very costly and time consuming. Further, having to apply for an exemption for each individual dosage form would be impracticable, time-consuming, and expensive for both manufacturers and FDA. Two comments asserted that subjecting homeopathic drug products to the new alcohol limitations would cause their removal from the market. One comment contended that to proceed with a rulemaking that has the effect of destroying an entire industry without the support of an economic impact analysis would contravene regulatory requirements.

The agency does not have sufficient data or information to determine whether orally ingested homeopathic drug products can be reformulated with 10 percent alcohol or less. Due to the manner in which homeopathic drug products are manufactured, the agency will not make a decision concerning the appropriate alcohol content of these products until it obtains the necessary data and information on how these products are manufactured and why they need such high levels of alcohol for product formulation. Rather than delay publication of this final rule, the agency will temporarily exempt orally ingested homeopathic drug products from the alcohol percentage limitations in § 328.10(b), (c), and (d). The agency will publish its decision concerning the appropriate alcohol content for orally ingested homeopathic drug products in a future issue of the **Federal Register**.

15. One comment suggested it would be more cost effective for industry and FDA to exempt herbal drugs that contain more than 50 percent herbal products on a weight to volume (w/v) basis, rather than require individual exemptions for herbal drug products that contain more than 10 percent alcohol by necessity.

The agency disagrees with the comment. The purpose of § 328.10 (e) is to exempt OTC drug products for which no alternatives to alcohol exist. The comment submitted no evidence to support why all herbal drug products that contain 50 percent (w/v) herbal ingredients should be automatically exempt.

16. One comment stated that the OTC drug product Aromatic Cascara Fluidextract, which contains 18 to 20 percent alcohol, cannot be formulated at lower alcohol concentrations because of its susceptibility to microbial contamination. The comment added that if the product were reformulated to 10 percent alcohol or less, it would not be within the specifications set forth in the United States Pharmacopeia (U.S.P.).

The comment is correct in stating that if Aromatic Cascara Fluidextract were

reformulated to 10 percent alcohol or less, it would not be within the specifications set forth in the U.S.P. Aromatic Cascara Fluidextract and Cascara Sagrada Fluidextract both contain between 18 and 20 percent alcohol (Ref. 1). The comment did not provide any data to substantiate that microbial contamination would occur if Aromatic Cascara Fluidextract were to be formulated at lower alcohol concentrations. Thus, the agency does not have sufficient data or information to determine whether Aromatic Cascara Fluidextract or Cascara Sagrada Fluidextract can be formulated with less alcohol.

The agency is currently working with the United States Pharmacopeial Convention (U.S.P.C.) to ascertain if a lower alcohol concentration can be used. Rather than delay publication of this final rule, the agency will temporary exempt Aromatic Cascara Fluidextract and Cascara Sagrada Fluidextract from the requirements in § 328.10(b), (c), and (d). The agency will publish its decision concerning the appropriate alcohol content for Aromatic Cascara Fluidextract and Cascara Sagrada Fluidextract in a future issue of the **Federal Register**.

Reference

(1) The United States Pharmacopeia 23—The National Formulary 18, United States Pharmacopeial Convention, Inc., Rockville, MD, pp. 282, 1994.

II. The Agency's Final Conclusions on OTC Drug Products Intended for Oral Ingestion that Contain Alcohol

The agency is issuing a final rule establishing the following limits on the concentrations of alcohol as an inactive ingredient in OTC drug products intended for oral ingestion: (1) 10 percent alcohol for products labeled for use by adults and children 12 years of age and over, (2) 5 percent alcohol for products labeled for use by children 6 to under 12 years of age, and (3) 0.5 percent alcohol for products labeled for use by children under 6 years of age. Further, the agency strongly recommends that OTC drug products for oral ingestion not contain any more than the minimum amount of alcohol necessary for use as a solvent, preservative, flavor (to enhance taste), or any other pharmaceutical purpose.

The agency concludes that the term ''alcohol free'' should mean no (0 percent) alcohol in a product. This requirement will assure consumers who want to purchase an OTC drug product with out alcohol that the product, in fact, contains no alcohol. The agency has determined that the alcohol content information should appear prominently and conspicuously on the principal display panel of the OTC drug product. This requirement is consistent with section 502(c) of the act (21 U.S.C. 352(c)). Further, because section 502(e) of the act requires that the quantity, kind, and proportion of alcohol be stated on a drug product's label, the alcohol content will also need to appear on the immediate container label when that container (e.g., a glass bottle) is marketed in another retail package, e.g., an outer box. This dual labeling of alcohol content will be beneficial should a consumer discard the outer package.

In accordance with the provisions found in § 328.10(e), the agency is temporarily exempting Aromatic Cascara Fluidextract, Cascara Sagrada Fluidextract, and orally ingested OTC homeopathic drug products from the requirements in § 328.10(b), (c), and (d). Additional information is needed about the formulations of these specific products. Rather than delay publication of this final rule to resolve the outstanding issues, the agency is temporarily exempting these products from some of the requirements. The agency will publish its decision concerning the appropriate alcohol content for Aromatic Cascara Fluidextract, Cascara Sagrada Fluidextract, and orally ingested homeopathic drug products in a future issue of the **Federal Register**. In the interim, these products must meet the labeling requirements in § 328.50.

III. Analysis of Impacts

An analysis of the cost and benefits of this regulation, conducted under Executive Order 12291, was discussed in the proposed rule (58 FR 54466 at 54470). Several comments concerning the reformulating, testing, repackaging, and relabeling of homeopathic drug products were received in response to the agency's request for specific comment on the economic impact of this rulemaking. The agency is temporarily exempting orally ingested homeopathic drug products from the requirements in § 328.10(b), (c), and (d) of this rulemaking. Therefore, no reformulation or testing will be necessary at this time. Any comments concerning a significant economic impact on reformulating or testing of orally ingested homeopathic drug products will be addressed in a future issue of the **Federal Register**. Homeopathic drug products will be subject to relabeling and repackaging, if necessary, in the same manner as other OTC drug products that contain alcohol and which are affected by this final rule. The burden on all products will be the same--the standard 1 year for relabeling to be done.

Executive Order 12291 has been superseded by Executive Order 12866. FDA has examined the impacts of the final rule under Executive Order 12866 and the Regulatory Flexibility Act (Pub. L. 96-354). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this final rule is consistent with the regulatory philosophy and principles identified in the Executive Order. In addition, the final rule is not a significant regulatory action as defined by the Executive Order and, thus, is not subject to review under the Executive Order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Within the OTC drug product marketplace, the agency is not aware of a significant number of products that would be affected due to their alcohol content as an inactive ingredient. Products that would be affected consist of a limited number of OTC liquid cough-cold, internal analgesic, laxative, and homeopathic drug products. The effect on orally ingested homeopathic drug products is discussed above, and these products have a partial exemption from the final rule. Accordingly, the agency certifies that the final rule will not have a significant economic impact on a substantial number of small entities. Therefore, under the Regulatory Flexibility Act, no further analysis is required.

IV. Environmental Impact

The agency has determined under 21 CFR 25.24(c)(6) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

List of Subjects in 21 CFR Part 328

Drugs, Labeling, Alcohol.

Therefore, under the Federal Food, Drug, and Cosmetic Act andunder authority delegated to the Commissioner of Food and Drugs, chapter I of title 21 of the Code of Federal Regulations is amended as follows:

1. Part 328 is added to read as follows:

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

Subpart A—General Provisions

Sec.

Subpart B—Ingredients

Subpart C—Labeling

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).

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

§ 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 Dockets Management Branch (HFA–305), Food and Drug Administration, rm. 1–23, 12420 Parklawn Dr., Rockville, MD 20857.

(f) 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.

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.

Dated: March 1, 1995,

William K. Hubbard,

Acting Deputy Commissioner for Policy.

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