21 CFR Part 331

[Docket No. 78N-0263]

Antacid Drug Products for Over-the-Counter Human Use; Final Classification of Category III Antacid Ingredients and Labeling Claims

AGENCY: Food and Drug Administration.

ACTION: Denial of petition and final decision.

SUMMARY: This notice denies a petition to amend the final monograph for over-the-counter (OTC) antacid drug products to include the ingredient alginic acid and the labeling claim "floating," and contains a final decision on the use of this ingredient and labeling claim for OTC antacid drug products. This notice is part of the ongoing review of OTC drug products conducted by FDA.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drugs and Biologics (HFN-210), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-295-8000.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of June 4, 1974 (39 FR 19862), FDA published the final monograph for OTC antacid drug products (21 CFR Part 331). Alginic acid was classified as a Category III ingredient and "floating" as a Category III labeling claim. At that time, OTC drug regulations in 21 CFR Part 330 provided for a 2-year period following the publication of a final monograph for manufacturers to conduct testing to upgrade Category III conditions (conditions for which there were insufficient data to determine general recognition of safety and effectiveness). During the testing period that had been established for OTC antacid drug products, a petition to amend the final monograph for OTC antacid drug products was submitted by Marion Laboratories, Inc., in support of its foam-forming floating antacid combination product containing the ingredients aluminum hydroxide dried gel, magnesium trisilicate, alginic acid, and sodium bicarbonate.

The Marion Laboratories' antacid combination product did not pass the in vitro effectiveness test set forth in the antacid final monograph (21 CFR 331.10(a)). The petition contained clinical studies in support of the product's antacid effectiveness and clarified the rationale for including alginic acid in the formulation, i.e., to react with the sodium bicarbonate in the formulation to form a foam that carries the antacid ingredients and floats on the stomach contents. The petition stated that no claim was being made that alginic acid has any antacid activity and that, therefore, alginic acid was an inactive ingredient. The petitioner called this product a foam-forming floating antacid.

In the **Federal Register** of September 5, 1978 (43 FR 39427), the agency published a final classification of Category III antacid ingredients and labeling cliams. All Category III ingredients and labeling claims except those covered by petitions to amend the antacid final monograph were reclassified in Category II (not generally recognized as safe and effective). Alginic acid and the labeling claim for "floating" were excluded from the agency's final classification of antacid conditions because the data contained in Marion Laboratories' petition were under review. The agency stated that its findings on the petition would be set forth in a future **Federal Register** publication following completion of its review of the data contained in the petition. In the interim, products affected by the pending petition were allowed to remain in the marketplace under 21 CFR 330.10(a).

After reviewing the petition, FDA informed Marion Laboratories, in a letter dated March 23, 1979, that the studies submitted were inadequate to support the effectiveness of its combination product. FDA suggested further clinical studies and provided Marion Laboratories with 2 years from the date of the letter to obtain and submit additional data demonstrating the product's effectiveness. The agency also stated that marketing of the product would be allowed to continue during the testing period (Ref. 1).

Not long after the above letter was issued, the United States District Court for the District of Columbia entered its opinion in *Cutler* v. *Kennedy*, 475 F. Supp. 838 (D.D.C. 1979). In this case, the plaintiffs alleged that 21 CFR 330.10 was unlawful because it authorized the marketing of Category III drugs after publication of a final monograph. The Court concluded that "* * * the FDA may not lawfully maintain Category III in any form in which drugs with Category III conditions * * * are exempted from enforcement action," (*Cutler, supra*, 475 F. Supp. at 856). The Court issued an order declaring the FDA OTC drug regulations, 21 CFR 330.10, unlawful to the extent that they authorize the marketing of Category III drugs after a final monograph. The Court also enjoined FDA from implementing any portion of the regulation that authorizes such marketing.

In conformance with the Court's decision, the agency established that any OTC drug product with a condition not included in Category I in a final OTC drug monograph was a new drug requiring an approved new drug application (NDA) as a condition of marketing. FDA then informed Marion Laboratories that its OTC antacid combination product containing alginic acid, which had been marketed under Category III conditions, was now considered a new drug without an approved NDA and that an NDA for the product should be submitted (Ref. 2).

In September 1981, Marion Laboratories submitted an NDA for two products containing alginic acid, i.e., Gaviscon Antacid Tablets and Gaviscon-2 Antacid Tablets. The agency found the data adequate to support the effectiveness of the products for the temporary relief of heartburn (acid indigestion) due to acid reflux, and the NDA was approved on December 9, 1983 (Ref. 3).

With this NDA approval, Marion Laboratories may now market the product without further consideration of the petition to amend the OTC antacid final monograph. However, the agency has not issued a final response to the original petition and has not completed action on the final classification of Category III ingredients and labeling claims excluded from the 1978 final classification (see above). In this notice, for the reasons given below, FDA denies Marion Laboratories' petition to amend the OTC antacid final monograph to include the combination product containing alginic acid and the "floating" labeling claim. Accordingly, the ingredient alginic acid and the term "floating" are not included in the final monograph for OTC antacid drug products.

As explained above, in its petition Marion Laboratories clarified that alginic acid is an inactive ingredient and no claims regarding antacid activity are made for this ingredient. Although originally reviewed as an active antacid ingredient, alginic acid is now classified as an inactive ingredient in OTC antacid drug product formulations and is labeled as such in marketed products. Because the OTC drug review establishes allowable active ingredients, not inactive ingredients, the agency will not consider this ingredient for inclusion in the antacid drug products monograph. Alginic acid, like any other inactive

ingredient, may be used in OTC drug formulations in compliance with the requirements for inactive ingredients set forth in 21 CFR 330.1(e), i.e., that they are safe and do not interfere with the effectiveness of the product or with tests to be performed on it.

Marion Laboratories' submission to the Advisory Review Panel on OTC Antacid Drug Products included labeling relating the property of "floating" to its product's effectiveness (Ref. 4). The Panel recognized that alginic acid-containing products may produce a layer of material floating on top of the contents of the stomach (April 5, 1973; 38 FR 8722), but concluded that there was insufficient evidence to support the claim that such a property contributed to the product's effectiveness (38 FR 8723). The agency notes that OTC drug monographs directly address only those labeling items that are related in a significant way to the safe and effective use of covered products by lay persons. These labeling items are the product statement of identity; names of active ingredients; indications for use; directions for use; warnings against unsafe use, side effects, and adverse reactions; and claims concerning mechanism of drug action. The agency considers the term "floating" to be a product attribute which describes a physical property. Normally, such product attributes are considered to be outside the scope of OTC drug monographs when the labeling does not relate the attribute to the effectiveness of the product. The agency has no objection to the use of terms describing product attributes of OTC drug product formulations as long as they do not imply that any therapeutic effect might occur, are not false or misleading, and are not intermixed with labeling established by the monograph. However, labeling relating "floating" to a product's antacid effectiveness, such as that submitted by Marion Laboratories, remains a condition which requires supporting data.

Marion Laboratories claimed that the property of floating added to the efficacy of its combination antacid drug product, i.e., that "floating" was more than simply a product attribute because it was directly related to effectiveness. Additional data in support of this claim were submitted by Marion Laboratories to the agency, and the NDA was approved. However, the contribution of the floating property as related to antacid effectiveness is not generally recognized. Therefore, in order to use labeling suggesting that "floating" uniquely contributes to an antacid's effectiveness, any other antacid drug product would need to have supporting data. Any interested person who believes that "floating" supports or enhances antacid effectiveness may submit an NDA or petition the agency to amend the final monograph for OTC antacid drug products. Such petition should include appropriate data to establish general recognition of safety and effectiveness, e.g., an appropriate in vitro or in vivo test.

The agency has examined the economic consequences of this notice in conjunction with other rules resulting from the OTC drug review. In a notice published in the **Federal Register** of February 8, 1983 (48 FR 5806), the agency announced the availability of an assessment of these economic impacts. The assessment determined that the combined impacts of all the rules resulting from the OTC drug review do not constitute a major rule according to the criteria established by Executive Order 12291. The agency therefore concludes that no one of these rules, including this notice for OTC antacid drug products, is a major rule.

The economic assessment also concluded that the overall OTC drug review was not likely to have a significant economic impact on a substantial number of small entities as defined in the Regulatory Flexibility Act, Pub. L. 96-354. That assessment included a discretionary Regulatory Flexibility Analysis in the event that an individual rule might impose an unusual or disproportionate impact on small entities. However, the requirement for a Regulatory Flexibility Analysis under the Regulatory Flexibility Act does not apply to this notice for OTC antacid drug products because the proposed rule was issued prior to January 1, 1981, and is therefore exempt.

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.

References

(1) Letter from J.R. Crout, FDA, to J.E. Budde, Marion Laboratories, Inc., dated March 23, 1979, coded LET, Docket No. 78N-0263, Dockets Management Branch.

(2) Letter from J.R. Crout, FDA to J.E. Budde, Marion Laboratories Inc., dated March 3, 1980, coded LET005, Docket No. 78N-0263, Dockets Management Branch.

(3) Letter from R. Temple, FDA, to J.E. Budde, Marion Laboratories, Inc., dated December 9, 1983, coded LET007, Docket No. 78N-0263, Dockets Management Branch.

(4) Copy of original labeling submitted to the Panel included in Docket No. 78N-0263, Docket Management Branch.

Dated: August 25, 1987.

John A. Norris,

Acting Commissioner of Food and Drugs.

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DEPARTMENT OF THE TREASURY

Internal Revenue Service

26 CFR Part 1

[T.D. 8158]

Income Taxes; Tax on Unearned Income of Certain Minor Children

AGENCY: Internal Revenue Service, Treasury.

ACTION: Temporary regulations.

SUMMARY: This document provides temporary regulations relating to the tax on unearned income of certain minor children. Changes to the applicable law were made by the Tax Reform Act of 1986. The regulations affect minor children who, at the close of the taxable year, have not attained age 14; have at least one living parent; and realize at least $1,000 of unearned income and provide the guidance needed to comply with the law.

DATES: The regulations are effective for taxable years beginning after December 31, 1986.

FOR FURTHER INFORMATION CONTACT: William A. Jackson of the Legislation and Regulations Division, Office of the Chief Counsel, Internal Revenue Service, 1111 Constitution Avenue NW., Washington, DC 20224, Attention: CC:LR:T (LR-112-86) (202) 566-4336, not a toll-free call.

SUPPLEMENTARY INFORMATION:

Background

This document contains temporary regulations relating to the tax on unearned income of certain minor children under section 1(i) of the Internal Revenue Code of 1986 (Code), as amended by section 1411 of the Tax Reform Act of 1986 (Pub. L. 99-514; 100 Stat. 2714).

These temporary regulations are presented in the form of questions and answers. Taxpayers may rely on these questions and answers for guidance. No inference, however, should be drawn regarding questions not addressed in the temporary regulations.