DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR PART 331

[Docket No. 88N-0003]

Antacid Drug Products for Over-the-Counter Human Use; Proposed Amendment to the Monograph

AGENCY: Food and Drug Administration.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Food and Drug Administration (FDA) is issuing a notice of proposed rulemaking to amend the final monograph for over-the-counter (OTC) antacid drug products to revise the conditions for marketing combination antacid/analgesic drug products, to add a section on the labeling of permitted combinations of active ingredients, and to redesignate the professional labeling section to conform to the format of other OTC drug final monographs. FDA is issuing this notice of proposed rulemaking after considering the report and recommendations of the Advisory Review Panel on OTC Internal Analgesic and Antirheumatic Drug Products and public comments on the advance notice of proposed rulemaking for OTC internal analgesic, antipyretic, and antirheumatic drug products that was based on those recommendations. The agency's proposal concerning OTC internal analgesic, antipyretic, and antirheumatic drug products is published elsewhere in this issue of the **Federal Register**. These proposals are part of the ongoing review of OTC drug products conducted by FDA.

DATE: Written comments or objections by March 16, 1989.

ADDRESS: Written comments or objections to the Dockets Management Branch (HFA-305), Food and Drug Administration, Room 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drug Evaluation and Research (HFD-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 issued a final monograph for OTC antacid drug products (21 CFR Part 331). Section 331.15(b) (21 CFR 331.15(b)) of the monograph provides for the combination of an antacid and any generally recognized as safe and effective analgesic ingredient(s) if the combination is indicated for use solely for concurrent symptoms, e.g., headache and acid indigestion, and is marketed in a form intended for ingestion as a solution. These combinations were limited to administration in solution because all the evidence of safety submitted for review under the rulemaking for OTC antacid drug products was derived from studies and experience with products administered as solutions (39 FR 19869).

Subsequent to the publication of the final rule for OTC antacid drug products, the Advisory Review Panel for OTC Internal Analgesic and Antirheumatic Drug Products (Internal Analgesic Panel) reviewed data on OTC antacid/analgesic combinations and recommended conditions for their safe and effective use in its report on OTC internal analgesic, antipyretic, and antirheumatic drug products (July 8, 1977; 42 FR 35346). This Panel recommended that acetaminophen could be combined with a Category I antacid ingredient provided the product was labeled for the concurrent symptoms involved, e.g., "For the temporary relief of occasional minor aches, pains, and headache, * * *, and for acid indigestion." The Panel did not specify any specific dosage form. The Panel also recommended as Category I an antacid/aspirin combination, labeled only for analgesic-antipyretic indications. However, in this case the combination was limited to marketing as a highly buffered aspirin for use as a solution (42 FR 35370).

In the tentative final monograph for OTC internal analgesic, antipyretic, and antirheumatic drug products published elsewhere in this issue of the **Federal Register**, FDA states for the first time its position on the establishment of a monograph for these drug products. In formulating its proposals on conditions for marketing combinations of antacid and analgesic ingredients in the internal analgesic, antipyretic, and antirheumatic drug products tentative final monograph, the agency considered the recommendations of both the Antacid Panel and the Internal Analgesic Panel as well as all currently-available data on such combinations. As discussed in comments 47, 76, 94, 95, and 96 of the tentative final monograph for OTC internal analgesic, antipyretic, and antirheumatic drug products, the agency has determined that (1) acetaminophen may be combined with any antacid ingredient(s) and may be labeled only for concurrent symptoms, (2) aspirin may be combined with any antacid ingredient(s) when marketed in a form intended for ingestion as a solution and may be labeled for concurrent symptoms as well as analgesic indications alone, and (3) combinations of other proposed generally recognized as safe and effective internal analgesic-antipyretic ingredients (i.e., carbaspirin calcium, choline salicylate, magnesium salicylate, and sodium salicylate) and antacid ingredients have not existed previously in the marketplace and lack supporting data.

Based on these findings, the agency has determined that the antacid final monograph should be updated to be consistent with the proposals being made in Part 343 (the internal analgesic, antipyretic, and antirheumatic tentative final monograph), published elsewhere in this issue of the **Federal Register**. Therefore, the agency is proposing to revise § 331.15(b) of the antacid monograph to read as follows:

(1) *Antacid and acetaminophen combinations.* See § 343.20(b)(1) of this chapter.

(2) *Antacid and aspirin combinations.* See § 343.20(b)(3) of this chapter.

In addition, the agency is proposing the addition of new § 331.60 to the antacid final monograph in order to provide for the labeling of permitted combinations of active ingredients and is redesignating the professional labeling section from § 331.31 to § 331.80 in accordance with the format of other recently published tentative final and final monographs for OTC drug products. Further, the agency is revising the *Scope* section (21 CFR 331.1) of the antacid final monograph in accordance with the format of other recently published monographs. Because of the interrelationship of this amendment to the antacid final monograph and the tentative final monograph for OTC internal analgesic, antipyretic, and antirheumatic drug products, the agency does not intend to finalize this amendment until the comments to the internal analgesic, antipyretic, and antirheumatic tentative final monograph have been fully evaluated.

The agency has examined the economic consequences of this proposed rulemaking 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 proposed rule 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, this particular rulemaking for OTC antacid drug products is not expected to pose such an impact on small businesses. Therefore, the agency certifies that this proposed rule, if implemented, will not have a significant economic impact on a substantial number of small entities.

The agency invites public comment regarding any substantial or significant economic impact that this rulemaking would have on OTC antacid drug products. Comments regarding the impact of this rulemaking on OTC antacid drug products should be accompanied by appropriate documentation.

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.

Interested persons may, on or before March 16, 1989, submit to the Dockets Management Branch (HFA–305), Food and Drug Administration, Rm. 4–62, 5600 Fishers Lane, Rockville, MD 20857, written comments or objections. Three copies of all comments or objections are to be submitted, except that individuals may submit one copy. Comments and objections are to be identified with the docket number found in brackets in the heading of this document and may be accompanied by a supporting memorandum or brief. Comments and objections may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

List of Subjects in 21 CFR Part 331

Antacid drug products, Labeling, Over-the-counter drugs.

Therefore, under the Federal Food, Drug, and Cosmetic Act and the Administrative Procedure Act, it is proposed that Subchapter D of Chapter I of Title 21 of the Code of Federal Regulations be amended in Part 331 as follows:

PART 331—ANTACID PRODUCTS FOR OVER-THE-COUNTER (OTC) HUMAN USE

1. The authority citation for Part 331 is revised to read as follows:

Authority: Secs. 201(p), 502, 505, 701, 52 Stat. 1041–1042 as amended, 1050–1053 as amended, 1055–1056 as amended by 70 Stat. 919 and 72 Stat. 948 (21 U.S.C. 321(p), 352, 355, 371); 5 U.S.C. 553; 21 CFR 5.10 and 5.11.

2. Section 331.1 is revised to read as follows:

§ 331.1 Scope.

(a) An over-the-counter antacid drug product in a form suitable for oral administration is generally recognized as safe and effective and is not misbranded if it meets each condition in this part and each general condition established in § 330.1 of this chapter.

(b) References in this part to regulatory sections of the Code of Federal Regulations are to Chapter I of Title 21 unless otherwise noted.

3. Section 331.15 is amended by revising paragraph (b) to read as follows:

§ 331.15 Combination with nonantacid active ingredients.

* * * * *

(b)(1) *Antacid and acetaminophen combinations.* See § 343.20(b)(1) of this chapter.

(2) *Antacid and aspirin combinations.* See § 343.20(b)(3) of this chapter.

* * * * *

4. Section 331.60 is added to Subpart D to read as follows:

§ 331.60 Labeling of permitted combinations of active ingredients.

Statements of identity, indications, warnings, and directions for use, respectively, applicable to each ingredient in the product may be combined to eliminate duplicative words or phrases so that the resulting information is clear and understandable.

(a) *Statement of identity.* For a combination drug product that has an established name, the labeling of the product states the established name of the combination drug product, followed by the statement of identity for each ingredient in the combination, as established in the statement of identity sections of the applicab1e OTC drug monographs. For a combination drug product that does not have an established name, the labeling of the product states the statement of identity for each ingredient in the combination, as established in the statement of identity sections of the applicable OTC drug monographs.

(b) *Indications.* The labeling of the product states, under the heading "Indications," the indication(s) for each ingredient in the combination, as established in the indications sections of the applicable OTC drug monographs, unless otherwise stated in this paragraph (b). Other truthful and nonmisleading statements, describing only the indications for use that have been established and listed in this paragraph may also be used, as provided in § 330.1(c)(2) of this chapter, 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.

(1) *For permitted combinations identified in § 331.15(b)(1).* The indications in § 343.60(b)(2) of this chapter should be used.

(2) *For permitted combinations identified in § 331.15(b)(2).* The indications in § 343.60(b)(4) of this chapter should be used.

(c) *Warnings.* The labeling of the product states, under the heading "Warnings," the warning(s) for each ingredient in the combination, as established in the warnings sections of the applicable OTC drug monographs.

(d) *Directions.* The labeling of the product states, under the heading "Directions," directions that conform to the directions established for each ingredient in the directions sections of the applicable OTC drug monographs, unless otherwise stated in this paragraph (d). When the time intervals or age limitations for administration of the individual ingredients differ, the directions for the combination product may not exceed any maximum dosage limits established for the individual ingredients in the applicable OTC drug monograph.

§ 331.31 [Redesignated as § 331.80]

5. Section 331.31 *Professional labeling* is redesignated as § 331.80.

Dated: August 5, 1988.

Frank E. Young,

Commissioner of Food and Drugs.

[FR Doc. 88–26156 Filed 11–15–88; 8:45 am]

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