DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 331

[Docket No. 88N–0327]

RIN 0905–AA06

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

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule that amends the monograph for over-the-counter (OTC) antacid drug products by deleting parts of the testing procedures in subpart C. This final rule is part of the ongoing review of OTC drug products conducted by FDA. Also, this final rule is part of the Administration's "Reinventing Government" initiative which seeks to streamline government and to ease the burden on regulated industry and consumers.

EFFECTIVE DATE: February 10, 1997.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drug Evaluation and Research (HFD–105), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–2304.

SUPPLEMENTARY INFORMATION:

I. Background

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) that included procedures for testing antacid drug products. An acid neutralizing capacity test is described in § 331.26. When the final monograph was issued in 1974, the United States Pharmacopeia (USP) did not include an acid neutralizing capacity test. However, in 1980 an acid neutralizing capacity test was included in the USP (Ref. 1). That test is substantially the same as the test found in the final monograph for OTC antacid drug products. Several revisions in the USP acid neutralizing capacity test have been made since 1980 to increase the accuracy and utility of the test. The current USP 23/National Formulary (N.F.) 18 acid neutralizing capacity test (Ref. 2) differs from the agency's antacid monograph testing procedures, which have not been revised.

The FDA recommended disintegration test method (in § 331.24) and the methods in current USP 23/N.F. 18 monographs for antacid tablets also have some differences. Current USP 23/N.F. 18 procedures include tests for powder and suspension dosage forms and for products having an acid neutralizing capacity greater than 25 milliequivalents (meq) of acid, as well as a more detailed sample preparation procedure for capsule dosage forms.

In the **Federal Register** of September 23, 1993 (58 FR 49826), the agency issued a notice of proposed rulemaking to amend the final monograph for OTC antacid drug products to delete parts of the testing procedures in subpart C, as discussed above in this document. The agency discussed the differences between its antacid monograph standards and those in the USP. The agency mentioned that it could amend its antacid monograph to be consistent with the USP, but opted to delete portions of its monograph testing procedures and refer to the USP procedures for determination of the antacid product's acid neutralizing capacity in place thereof. The agency noted that USP procedures do not include a "preliminary antacid test" (as contained in § 331.25 of the antacid monograph) or a procedure for the "determination of percent contribution of active ingredients" in a combination antacid drug product (as contained in § 331.21 of the antacid monograph). The agency does not consider the "preliminary antacid test" as essential to the determination of a product's acid neutralizing capacity. However, manufacturers may elect to continue to use this test as a preliminary screening procedure. The agency stated that it was retaining § 331.21 ("*determination of percent contribution of active ingredients*") in the monograph (redesignated as § 331.20) so that a procedure will be available for making that determination. No comments were received in response to the agency's proposed changes in the antacid monograph.

References

(1) "United States Pharmacopeia XX—National Formulary XV," United States Pharmacopeial Convention, Inc., Rockville, MD, p. 912, 1980.

(2) "United States Pharmacopeia 23—National Formulary 18," United States Pharmacopeial Convention, Inc., Rockville, MD, pp. 54–55 and 1791–1793, 1994.

II. The Agency's Final Conclusions on the Amendment to the Monograph for OTC Antacid Drug Products

In the proposal, the agency referred to the acid neutralizing capacity test procedures in USP XXII/N.F. XVII. Since the proposal was published, USP 23/N.F. 18 became official on January 1, 1995. The test procedures in both editions of the USP are the same. Therefore, the agency is referencing USP 23/N.F. 18 in this final rule.

The agency is removing the following sections from "Subpart C—Testing Procedures" in "Part 331—Antacid Products for Over-the-Counter (OTC) Human Use": §§ 331.20, 331.22, 331.23, 331.24, 331.25, and 331.26. The agency is redesignating § 331.21 as § 331.20 and amending it to refer to the USP 23/N.F. 18 test procedure in place of § 331.26, which is being removed. The agency is retaining § 331.29 ("*test modifications*") in case there is a need for any manufacturer to petition for a test modification, is redesignating this section as § 331.21, and is amending it to reference the USP 23/N.F. 18 test procedure. The agency is also amending §§ 331.10(a) and 331.80(a)(1) to refer to USP 23/N.F. 18.

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 49826 at 49827). No comments were received in response to the agency's request for specific comment on the economic impact of this rulemaking. Executive Order 12291 has been superseded by Executive Order 12866.

FDA has examined the impacts of this 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. Manufacturers of OTC antacid drug products should not be affected by the deletion of certain testing procedures that have already been incorporated into the USP/N.F. 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 331

Labeling, Over-the-counter drugs.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 331 is amended as follows:

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

1. The authority citation for 21 CFR part 331 continues to read as follows:

Authority: Secs. 201, 501, 502, 503, 505, 510, 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 351, 352, 353, 355, 360, 371).

2. Section 331.10 is amended by revising paragraph (a) to read as follows:

31.10 Antacid active ingredients.

(a) The active antacid ingredients of the product consist of one or more of the ingredients permitted in § 331.11 within any maximum daily dosage limit established, each ingredient is included at a level that contributes at least 25 percent of the total acid neutralizing capacity of the product, and the finished product contains at least 5 meq of acid neutralizing capacity as measured by the procedure provided in the United States Pharmacopeia 23/National Formulary 18. The method established in § 331.20 shall be used to determine the percent contribution of each antacid active ingredient.

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§ 331.20 [Removed]

3. Section 331.20 *Apparatus and reagents* is removed from subpart C.

§ 331.21 [Redesignated as § 331.20]

4. Section 331.21 is redesignated as § 331.20 and revised to read as follows:

§ 331.20 Determination of percent contribution of active ingredients.

To determine the percent contribution of an antacid active ingredient, place an accurately weighed amount of the antacid active ingredient equal to the amount present in a unit dose of the product into a 250-milliliter (mL) beaker. If wetting is desired, add not more than 5 mL of alcohol (neutralized to an apparent pH of 3.5), and mix to wet the sample thoroughly. Add 70 mL of water, and mix on a magnetic stirrer at 300±30 r.p.m. for 1 minute. Analyze the acid neutralizing capacity of the sample according to the procedure provided in the United States Pharmacopeia 23/National Formulary 18 and calculate the percent contribution of the antacid active ingredient in the total product as follows:

Percent contribution = (Total meq. Antacid Active Ingredient x100)/(Total meq. Antacid Product).

§ 331.22 [Removed]

5. Section 331.22 *Reagent standardization* is removed.

§ 331.23 [Removed]

6. Section 331.23 *Temperature standardization* is removed.

§ 331.24 [Removed]

7. Section 331.24 *Tablet disintegration test* is removed.

§ 331.25 [Removed]

8. Section 331.25 *Preliminary antacid test* is removed.

§ 331.26 [Removed]

9. Section 331.26 *Acid neutralizing capacity test* is removed.

§ 331.29 [Redesignated as § 331.21]

10. Section 331.29 is redesignated as § 331.21 and revised to read as follows:

§ 331.21 Test modifications.

The formulation or mode of administration of certain products may require a modification of the United States Pharmacopeia 23/National Formulary 18 acid neutralizing capacity test. Any proposed modification and the data to support it shall be submitted as a petition under the rules established in § 10.30 of this chapter. All information submitted will be subject to the disclosure rules in part 20 of this chapter.

11. Section 331.80 is amended by revising paragraph (a)(1) to read as follows:

§ 331.80 Professional labeling.

(a) * * *

(1) Shall contain the neutralizing capacity of the product as calculated using the procedure set forth in United States Pharmacopeia 23/National Formulary 18 expressed in terms of the dosage recommended per minimum time interval or, if the labeling recommends more than one dosage, in terms of the minimum dosage recommended per minimum time interval.

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Dated: January 29, 1996.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

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