DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 310

[Docket No. 79N-0176]

Stomach Acidifier Drug Products for Over-the-Counter Human Use

AGENCY: Food and Drug Administration.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Food and Drug Administration (FDA) is issuing a notice of proposed rulemaking that would establish that over-the-counter (OTC) stomach acidifier drug products are not generally recognized as safe and effective and are misbranded. FDA is issuing this notice of proposed rulemaking after considering the report and recommendations of the Advisory Review Panel on OTC Miscellaneous Internal Drug Products and public comments on an advance notice of proposed rulemaking that was based on those recommendations. This proposal is part of the ongoing review of OTC drug products conducted by FDA.

DATES: Written comments, objections, or requests for oral hearing on the proposed regulation before the Commissioner of Food and Drugs by May 15, 1985. New data by January 15, 1986. Comments on the new data by March 17, 1986. These dates are consistent with the time periods specified in the agency's revised procedural regulations for reviewing and classifying OTC drugs (21 CFR 330.10). Written comments on the agency's economic impact determination by May 15, 1985.

ADDRESS: Written comments, objections, new data, or requests for oral hearing to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Willaim E. Gilbertson, Center for Drugs and Biologics (HFN-210), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-4960.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of October 19, 1979 (44 FR 60316), FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking that would classify OTC stomach acidifier drug products as not generally recognized as safe and effective and as being misbranded and would declare these products to be new drugs within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321(p)). The notice was based on the recommendations of the Advisory Review Panel on OTC Miscellaneous Internal Drug Products, which was the advisory review panel responsible for evaluation data on the active ingredients in this drug class. Interested persons were invited to submit comments by January 17, 1980. Reply comments in response to comments filed in the initial comment period could be submitted by February 18, 1980.

In accordance with § 330.10(a)(10), the data and information considered by the Panel were put on public display in the Dockets Management Branch (HFA-305), Food and Drug Administration (address above), after deletion of a small amount of trade secret information. In response to the advance notice of proposed rulemaking, two drug manufacturers and one college of pharmacy submitted comments. These comments received are on public display in the Dockets Management Branch.

In this proposed rule to amend Part 310 by adding to Subpart E new § 310.540 (21 CFR 310.540), FDA states for the first time its position on OTC stomach acidifier drug products. Final agency action on this matter will occur with the publication at a future date of a final rule relating to OTC stomach acidifier drug products.

This proposal constitutes FDA's tentative adoption of the Panel's conclusions and recommendations on OTC stomach acidifier drug products, based on the comments received and the agency's independent evaluation of the Panel's report. As discussed in the final rule revising the procedural regulations for reviewing and classifying OTC drugs, FDA will no longer use the terms "Category I" (generally recognized as safe and effective and not misbranded), "Category II" (not generally recognized as safe and effective or misbranded), and "Category III" (available data are insufficient to classify as safe and effective, and further testing is required) at the final rule, but will use instead the terms "monograph conditions" (old Category I) and "nonmonograph conditions" (old Categories II and III). (See the **Federal Register** of September 29, 1981; 46 FR 47730.) This document retains the concepts of Categories I, II, and III at the proposed rule stage.

In the advance notice of proposed rulemaking, the agency stated that if it proposed to adopt the Panel's recommendation it would propose that stomach acidifier drug products be eliminated from the OTC market effective 6 months after the date of publication of a final rule in the **Federal Register**, regardless of whether further testing was undertaken to justify their future use. Based on all information available to date, the agency is proposing that stomach acidifiers as a class of drugs be found to be ineffective. If this proposed finding is adopted in the final rule, the agency advises that the conditions under which the drug products that are subject to this rule are not generally recognized as safe and effective and are misbranded (nonmonograph conditions) will be effective 6 months after the date of publication of the final rule in the **Federal Register**. On or after that date, no OTC drug products that are subject to the rule may be initially introduced or initially delivered for introduction into interstate commerce unless they are the subject of an approved new drug application (NDA). Manufacturers are encouraged to comply voluntarily with the proposed rule at the earliest possible date.

All "OTC Volumes" cited throughout this document refer to the submissions made by interested persons pursuant to the call-for-data notices published in the **Federal Register** of November 16, 1973 (38 FR 31696) and August 27, 1975 (40 FR 38179). The volumes are on public display in the Dockets Management Branch.

I. The Agency's Tentative Conclusions on the Comments

1. One comment requested that the statement "the basal rate is almost 30 milliliters (mL) of a dilute solution of hydrochloric acid per hour," in the Panel's discussion of stomach physiology (44 FR 60318), be clarified to read "30 mL of gastric fluid." The comment contended that the phrase "dilute solution of hydrochloric acid" could be mistaken to mean "diluted hydrochloric acid, USP," which would contain more pure hydrochloric acid than that which is available from the same amount of gastric fluid.

The agency agrees that the statement referred to by the comment could be misinterpreted. The agency believes that a less ambiguous statement reflecting the Panel's intended meaning would be as follows: "the basal rate is almost 30 mL of gastric fluid per hour."

2. Two comments disagreed with the Panel's conclusions that the conditions of achlorhydria and hypochlorhydria are asymptomatic and not amenable to self-diagnosis, and that no OTC stomach acidifier active ingredient is generally recognized as effective in treating these conditions. The comments asserted that submitted data showed that achlorhydria is accompanied by recognizable symptoms such as gas, diarrhea, abdominal distention, nausea,

and vomiting. The comments added that even if this condition is asymptomatic, the Panel's concern about self-diagnosis is unwarranted because OTC stomach acidifiers are generally used only after consultation with a doctor. The comments proposed that stomach acidifiers be available OTC with labeling recommending their use only on the advice of a doctor or other health professional. The comments pointed out that such an approach was recommended by the same Panel in the advance notice of proposed rulemaking for OTC exocrine pancreatic insufficiency drug products (44 FR 75669). To support the effectiveness of stomach acidifiers, one of the comments discussed several published studies and other information previously submitted to the Panel (Refs. 1 through 12). Similarly, the other comment argued that the Panel did not adequately consider or respond to the submitted data, specifically citing published studies, extracts from medical texts, and affidavits from five gastroenterologists and two hematologists (Refs. 13, 14, and 15).

The comments predicted that diluted hydrochloric acid, USP, will continue to be used by doctors to treat achlorhydria and hypochlorhydria even if OTC stomach acidifier drug products are removed from the market, and added that removal of these stomach acidifier drug products will eliminate a form of therapy that is safer than the use of diluted hydrochloric acid, USP.

After evaluating the data reviewed by the Panel and the additional information presented in the comments, FDA concludes that achlorhydria and hypochlorhydria are not established medical conditions causing any specific symptoms that require treatment. The data and information cited by the comments were also considered by the Panel. The Panel determined, and the agency concurs, that the data and information do not provide sufficient evidence that these conditions require treatment. Although hydrochloric acid replacement therapy has traditionally been used in the conditions of achlorhydria and hypochlorhydria, there are no adequate and well-controlled studies to demonstrate that administration of hydrochloric acid has any therapeutic value in either condition. This same conclusion was reached by the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, for drugs containing glutamic acid hydrochloride (Ref. 16). Moreover, recent evaluations of hydrochloric acid therapy in recognized pharmacology texts also concur with the Panel's findings. For example, in the sixth edition of the Pharmacological Basis of Therapeutics, Harvey indicates that definitive clinical evidence of hydrochloric acid's effectiveness is lacking and reports of positive results may be based upon a placebo effect (Ref. 17). The fourth edition of AMA Drug Evaluations concludes that there are no established indications for hydrochloric acid, and the fifth edition of the Review of Medical Pharmacology likewise notes that the consensus now is that the use of hydrochloric acid as a replacement therapy in patients with achlorhydria or hypochlorhydria is not an accepted indication (Refs. 18 and 19). Therefore, the agency concludes that any ingredient recommended for stomach acidifier use is Category II.

The comments' recommendation to label the products for use only upon the advice of a doctor does not remedy the failure to have adequate evidence of safety and effectiveness. No stomach acidifier active ingredient has been shown to be generally recognized as safe and effective in treating achlorhydria and hypochlorhydria. Nor are there recognizable symptoms of these conditions that may properly be treated with an OTC drug product. Although such an approach was used in the advance notice of proposed rulemaking for OTC exocrine pancreatic insufficiency drug products, in that case the Panel classified two active ingredients as generally recognized as safe and effective and the Panel believed that the condition of exocrine pancreatic insufficiency could be self-treated because of recognizable sysptoms.

References

(1) Sharp, G.S., and J.W. Hazlet, "Evaluation of a New Method for Supplementation of Gastric Hydrochloric Acid," *American Journal of Digestive Diseases*, 21:140–144, 1954.

(2) Bloomfield, A.L., and W.S. Polland, "Gastric Anacidity; Its Relations to Disease," The Macmillan Co., New York, pp. 1–175, 1933.

(3) Rudick, J., and H.D. Janowitz, "Gastric Physiology," *in* "Gastroenterology," 3d Ed., edited by H.L. Bockus, W.B. Saunders Co., Philadelphia, pp. 405–418, 1974.

(4) Faber, K., and G. Lange, "Pathogenesis and Etiology of Chronic Achylia," *Zeitschrift fur Klinische Medizin*, 66:53–89, 1908.

(5) DeVoe, R. W., and L. E. Moses, "Iron Therapy in Pregnancy; A Comparative Study of Various Modes," *California Medicine*, 81:304–307, 1954.

(6) Strauss, M. B., and W. B. Castle, "Studies of Anemia in Pregnancy. I. Gastric Secretion in Pregnancy and the Puerperium," *American Journal of the Medical Sciences*, 184:655–662, 1932.

(7) Strauss, M. B., and W. B. Castle, "Studies of Anemia in Pregnancy. II. The Relationship of Dietary Deficiency and Gastric Secretion to Blood Formation During Pregnancy," *American Journal of the Medical Sciences*, 184:663–673, 1932.

(8) Harvey, S. C., "Gastric Antacids and Digestants," *in* "The Pharmacological Basis of Therapeutics," edited by L. S. Goodman and A. Gilman, the Macmillan Co., New York, p. 1002, 1970.

(9) Aviado, D. M., "Pharmacologic Principles of Medical Practice," 6th Ed., Williams and Wilkens Co., Baltimore, pp. 917–923, 1972.

(10) Sharp, G. S., "The Diagnosis and Treatment of Achlorhydria; Preliminary Report of New Simplified Methods," *Western Journal of Surgery, Obstetrics and Gynecology*, 61:353–360, 1953.

(11) Williams, J., "The Effect of Ascorbic Acid on Iron Absorption in Post-Gastrectomy Anaemia and Achlorhydria," *Clinical Science*, 18:521, 1959.

(12) Wintrobe, M.M., "Clinical Hematology," 4th Ed., Lea and Febiger, Philadelphia, p. 134, 1956.

(13) OTC Volume 170103.

(14) OTC Volume 170104.

(15) OTC Volume 170124.

(16) NAS–NRC Report on Aclor Capsules (NDA 4–484), copy included in OTC Volume 17ATFM.

(17) Harvey, S. C., "Gastric Antacids and Digestants," *in* "The Pharmaceutical Basis of Therapeutics," edited by L. S. Goodman and A. Gilman, the Macmillan Co., New York, p. 970, 1980.

(18) "AMA Drug Evaluations," 4th Ed., Publishing Sciences Group, Inc., Littleton, MA, p. 1008, 1980.

(19) Meyers, F. H., E. Jawetz, and A. Goldfien, "Review of Medical Pharmacology," 5th Ed., Lange Medica; Publication, Los Altos, CA, p. 322, 1976.

3. One comment stated that a combination stomach acidifier drug product containing betaine hydrochloride and pepsin, which was reviewed by the Panel, is useful in replenishing pepsin in cases of gastric achylia, a condition in which the stomach fails to secrete hydrochloric acid and pepsin. Gastric achylia is often found in patients with pernicious anemia or gastric carcinoma. The comment requested that the combination product be classified in Category I, but added that "at a minimum, the final monograph should be deferred and acidifiers at least allowed to remain on the market pending an opportunity to conduct and complete further studies to evaluate their effectiveness."

The agency agrees with the Panel that the combination of betaine hydrochloride and pepsin is not generally recognized as effective in treating achlorhydria and hypochlorhydria. As discussed in comment 2 above, the agency concludes

that no ingredient is generally recognized as safe and effective for treating these conditions. Pepsin replacement therapy is not within the scope of this document. Pepsin was reviewed by the Advisory Review Panel on OTC Miscellaneous Internal Drug Products for use as an OTC digestive aid and judged to be not generally recognized as effective for the treatment of symptoms of either immediate postprandial upper abdominal distress or intestinal distress. (See the **Federal Register** of January 5, 1982; 47 FR 467 and 479.) The agency's position on the status of pepsin for use as a digestive aid will be initially stated when the tentative final monograph on OTC digestive aid drug products is published in a future issue of the **Federal Register.**

The comment's request that the final rule be deferred to permit additional studies to be conducted is unjustified. In the **Federal Register** of September 29, 1981 (46 FR 47730), FDA set forth revised procedural regulations for reviewing and classifying OTC drugs. This final rule revised the time period during which new data may be submitted without petition to FDA to support the inclusion in a final monograph of a condition not classified in Category I in a proposed monograph or tentative final monograph. Submission of data without petition is permitted until 12 months after publication of a tentative final monograph (21 CFR 330.10(a)(7)(iv)). New data submitted after that time will be considered only after the final monograph has been published unless the Commissioner finds that good cause warrants earlier consideration (21 CFR 330.10(a)(7)(v)). The agency will not delay a rulemaking proceeding so that additional studies may be conducted. In the case of stomach acidifier drug products, manufacturers have been aware of the Panel's recommendations at least since October 1979. Therefore, manufacturers have had ample opportunity to conduct studies and to submit new data.

4. One comment, referring to a product containing glutamic acid hydrochloride, and another comment, referring to a product containing betaine hydrochloride and pepsin, claimed that these products were exempt from the "new drug" provisions of section 201(p) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321(p)) under the "grandfather" provisions of the 1938 act and the 1962 amendments to the act. The comments stated that each product was marketed prior to 1938, that only insubstantial changes have been made in formulation and labeling since that time, and that the products' current labeling contains the same representations for use that were contained in the labeling used before 1938. The comments concluded that each product was a "grandfathered" product not subject to this regulation.

To qualify for exemption from the "new drug" definition under the 1938 grandfather clause, the drug product must have been subject to the Food and Drug Act of 1906, prior to June 25, 1938, and at such time its labeling must have contained the same representations concerning the conditions of its use (21 U.S.C. 321(p)(1)). Under the 1962 grandfather clause, a drug product which preceding October 9, 1962, (1) was commercially used or sold in the United States, (2) was not a "new drug" as defined in the 1938 act, and (3) was not covered by an approved NDA under the 1938 act, would not be subject to the added requirement of effectiveness "when intended solely for use under conditions prescribed, recommended, or suggested in the labeling with respect to such drugs." Pub. L. 87-781, section 701(c)(4), 76 Stat. 788, note following 21 U.S.C. 321.

The person seeking to show that a drug comes within a grandfather exemption must prove every essential fact necessary for invocation of the exemption. See *United States* v. *An Article of Drug * * * "Bentex Ulcerine,"* 469 F.2d 875, 878 (5th Cir. 1972), *cert. denied,* 412 U.S. 938 (1973). Furthermore, the grandfather clause will be strictly construed against one who invokes it. See id.; *United States* v. *Allan Drug Corp.,* 357 F.2d 713, 718 (10th Cir.), *cert. denied,* 385 U.S. 899 (1966).

A change in composition or labeling precludes the applicability of the grandfather exemption. *See USV Pharmaceutical Corp. v. Weinberger,* 412 U.S. 655, 663 (1973). The firm concedes that minor changes have been made in the labeling and formulation of the glutamic acid hydrochloride product since it was first marketed, prior to 1938. In any event, the evidence shows that both the labeling and the composition of the product have changed since passage of the 1938 act. Therefore, the product fails to qualify for the 1938 grandfather exemption.

In order to qualify for the 1962 grandfather exemption, it must be proven, among other things, that the product was generally recognized among qualified experts as safe for its intended uses (i.e., it was not a "new drug" under the 1938 act) and that the product was not covered by an approved NDA. The glutamic acid hydrochloride product was labeled for the treatment of achlorhydria, pernicious anemia, and gastric carcinoma. There are no adequate and well-controlled studies showing that the glutamic acid hydrochloride product is safe for use in pernicious anemia or gastric carcinoma. The product is not now, and never has been, generally recognized by qualified experts as safe for these recommended uses. Furthermore, the product (as a "me-too" product) was covered by an effective NDA as of October 9, 1962, within the meaning of the grandfather clause. *See USV Pharmaceutical Corp.* v. *Weinberger,* 412 U.S. 655 (1973). Therefore, the glutamic acid hydrochloride product fails on at least two grounds to qualify for the 1962 grandfather exemption.

No evidence was submitted to the agency to show that the labeling and composition of the betaine hydrochloride product have remained unchanged since either 1938 or 1962. Without such evidence, the product cannot qualify for either grandfather exemption. The manufacturer has suggested that FDA should search for evidence to support the company's grandfather claim. However, the burden of proof with respect to the grandfather exemption is not on FDA, but on the person seeking the exemption. *See An Article of Drug * * * "Bentex Ulcerine," supra; Upjohn* v. *Finch, supra.*

In any event, the 1938 and 1962 grandfather clauses apply only to the new drug provisions of the act and not to the adulteration and misbranding provisions. The OTC drug review was designed to implement both the misbranding and the new drug provisions of the act. (See 21 CFR 330.10; 37 FR 9466 (May 11, 1972) (comment 23).) The grandfather clauses do not preclude the agency from reviewing any currently marketed OTC drug, regardless of whether it has grandfather protection from the new drug provisions, in order to ensure that the drug is not misbranded. The agency concludes that the product referred to by the comments are subject to this proposed rulemaking.

II. The Agency's Tentative Adoption of the Panel's Report

FDA has considered the comments and other relevant data and information available at this time and concludes that it will tentatively adopt the Panel's report and recommendation that betaine hydrochloride, glutamic acid hydrochloride, diluted hydrochloric acid, and pepsin labeled for use as OTC stomach acidifiers are classified Category II.

The agency is also revising § 310.540 to clarify that a product covered by the

regulation is a new drug for which an approved NDA is required for marketing, and in the absence of an approved NDA the product would also be misbranded under section 502 of the act.

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 stomach acidifier drug products, is a major rule.

For purposes of the Regulatory Flexiblity Act, the economic assessment concluded that, while the average economic impact of the overall OTC drug review on small entities will not be significant, the possibility of larger-than-average impacts some small firms in some years might exist. Therefore, the assessment included a discretionary Regulatory Flexibility Analysis in the event that an individual rule might impose a significant impact on a substantial number of small entities. The analysis identified the possibilities of reducing burdens on small firms through the use of (a) relaxed safety and efficacy standards or (b) labels acknowledging unproven safety or efficacy. However, the analysis concluded that there is no legal basis for any preferential waiver, exemption, or tiering strategy for small firms compatible with the public health requirements of the Federal Food, Drug, and Cosmetic Act. Nevertheless, to avoid overlooking any problems or feasible possibilities of relief peculiar to this group of products, the agency invites public comment regarding any substantial or significant economic impact that this rulemaking would have on OTC stomach acidifier drug products. Comments regarding the economic impact of this rulemaking should be accompanied by appropriate documentation. Because the agency has not previously invited specific comment on the economic impact of the OTC drug review on OTC stomach acidifier drug products, a period of 120 days from the date of publication of this proposed rulemaking in the **Federal Register** will be provided for comments on this subject to be developed and submitted. The agency will evaluate any comments and supporting data that are received and will reassess the economic impact of this rulemaking in the preamble to the final rule.

The agency has determined that under 21 CFR 25.24(d)(9) (proposed in the **Federal Register** of December 11, 1979; 44 FR 71742) this proposal is of a type that does not individually or cumulatively have a significant impact on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

List of Subjects in 21 CFR Part 310

New drugs.

Therefore, under the Federal Food, Drug, and Cosmetic Act (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)), and the Administrative Procedure Act (secs. 4, 5, and 10, 60 Stat. 238 and 243 as amended (5 U.S.C. 553, 554, 702, 703, 704)), and under 21 CFR 5.11, it is proposed that Subchapter D of Chapter I of Title 21 of the Code of Federal Regulations be amended in Part 310 by adding to Subpart E new § 310.540, to read as follows:

PART 310—[AMENDED]

§ 310.540 Drug products containing active ingredients offered over-the-counter (OTC) for use as stomach acidifiers.

(a) Betaine hydrochloride, glutamic acid hydrochloride, diluted hydrochloride acid, and pepsin have been present as ingredients in over-the-counter (OTC) drug products for use as stomach acidifiers. Because of the lack of adequate data to establish the effectiveness of these or any other ingredients for use in treating achlorhydria and hypochlorhydria, and because such conditions are asymptomatic, any OTC drug product containing ingredients offered for use as a stomach acidifer cannot be considered generally recognized as safe and effective.

(b) Any OTC drug product that is labeled, represented, or promoted for use as a stomach acidifier is regarded as a new drug within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act, for which an approved new drug application under section 505 of the act and Part 314 of this chapter is required for marketing. In the absence of an approved new drug application, such product is also misbranded under section 502 of the act.

(c) A completed and signed "Notice of Claimed Investigational Exemption for a New Drug" (Form FDA–1571) (OMB Approval No. 0910–0014), as set forth in § 312.1 of this chapter, is required to cover clinical investigations designed to obtain evidence that any drug product labeled, represented, or promoted as a stomach acidifier for OTC use is safe and effective for the purpose intended.

(d) After the effective date of the final regulation, any such OTC drug product initially introduced or initially delivered for introduction into interstate commerce that is not in compliance with this section is subject to regulatory action.

Interested persons may, on or before May 15, 1985, submit to the Dockets Management Branch (HFA–305), Food and Drug Administration, Rm. 4–62, 5600 Fishers Lane, Rockville, MD 20857, written comments, objections, or requests for oral hearing before the Commissioner. A request for an oral hearing must specify points to be covered and time requested. The agency has provided this 120 day period (instead of the normal 60 days) because of the number of OTC drug review documents being published concurrently. Written comments on the agency's economic impact determination may be submitted on or before May 15, 1985. Three copies of all comments, objections, and requests are to be submitted, except that individuals may submit one copy. Comments, objections, and requests 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, objections, and requests may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday. Any scheduled oral hearing will be announced in the **Federal Register**.

Interested persons, on or before January 15, 1986, may also submit in writing new data demonstrating the safety and effectiveness of those conditions not classified in Category I. Written comments on the new data may be submitted on or before March 17, 1986. These dates are consistent with the time periods specified in the agency's final rule revising the procedural regulations for reviewing and classifying OTC drugs, published in the **Federal Register** of September 29, 1981 (46 FR 47730). Three copies of all data and comments on the data are to be submitted, except that individuals may submit one copy, and all data and comments are to be identified with the docket number found in brackets in the heading of this document. Data and comments should be addressed to the Dockets Management Branch (HFA–305) (address above). Received data and

comments may also be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

In establishing a final rule, the agency will ordinarily consider only data submitted prior to the closing of the administrative record on March 17, 1986. Data submitted after the closing of the administrative record will be reviewed by the agency only after a final rule is published in the **Federal Register** unless the Commissioner finds good cause has been shown that warrants earlier consideration.

Dated: December 31, 1984.

Frank E. Young,

Commissioner of Food and Drugs.

Margaret M. Heckler,

Secretary of Health and Human Services.

[FR Doc. 85-678 Filed 1-14-85; 8:45 am]

BILLING CODE 4160-01-M