

IV. Analysis of Impacts

An analysis of the costs and benefits of this regulation, conducted under Executive Order 12291 was discussed in the proposed rule (56 FR 32282 at 32289). Comments received were discussed in part II of this final rule. Executive Order 12291 has been superseded by Executive Order 12866.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, so, 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. This final rule will result in the removal of all drug products containing the ingredients pancreatin and pancrelipase from the OTC marketplace. However, only a limited number of OTC drug products are marketed in this manner and are affected by this 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.

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 310

Administrative practice and procedure, Drugs, Labeling, Medical devices, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under

authority delegated to the Commissioner of Food and Drugs, 21 CFR part 310 is amended as follows:

PART 310—NEW DRUGS

1. The authority citation for 21 CFR part 310 continues to read as follows:

Authority: Secs. 201, 301, 501, 502, 503, 505, 506, 507, 512-516, 520, 601(a), 701, 704, 705, 721 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 331, 351, 352, 353, 355, 356, 357, 360b-360f, 360j, 361(a), 371, 374, 375, 379(e); secs. 215, 301, 302(a), 351, 354-360F of the Public Health Service Act (42 U.S.C. 216, 241, 242(a), 262, 263b-263n).

2. New § 310.543 is added to subpart E to read as follows:

§ 310.543 Drug products containing active ingredients offered over-the-counter (OTC) for human use in exocrine pancreatic insufficiency.

(a) Hemicellulase, pancreatin, and pancrelipase have been present as ingredients in exocrine pancreatic insufficiency drug products. Pancreatin and pancrelipase are composed of enzymes: amylase, trypsin (protease), and lipase. Significant differences have been shown in the bioavailability of marketed exocrine pancreatic insufficiency drug products produced by different manufacturers. These differences raise a potential for serious risk to patients using these drug products. The bioavailability of pancreatic enzymes is dependent on the process used to manufacture the drug products. Information on this process is not included in an OTC drug monograph. Therefore, the safe and effective use of these enzymes for treating exocrine pancreatic insufficiency cannot be regulated adequately by an OTC drug monograph. Information on the product's formulation, manufacture, quality control procedures, and final formulation effectiveness testing are necessary in an approved application to ensure that a company has the ability to manufacture a proper bioactive formulation. In addition, continuous physician monitoring of patients who take these drug products is a collateral measure necessary to the safe and effective use of these enzymes, causing such products to be available by prescription only.

(b) Any drug product that is labeled, represented, or promoted for OTC use in the treatment of exocrine pancreatic insufficiency is regarded as a new drug

within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act (the act), for which an approved application under section 505 of the act and part 314 of this chapter is required for marketing. In the absence of an approved application, such product is also misbranded under section 502 of the act.

(c) Clinical investigations designed to obtain evidence that any drug product labeled, represented, or promoted for OTC use in the treatment of exocrine pancreatic insufficiency is safe and effective for the purpose intended must comply with the requirements and procedures governing the use of investigational new drugs set forth in part 312 of this chapter.

(d) After May 7, 1991, any such OTC drug product that contains hemicellulase initially introduced or initially delivered for introduction into interstate commerce that is not in compliance with this section is subject to regulatory action.

(e) After October 24, 1995, any such OTC drug product that contains pancreatin or pancrelipase initially introduced or initially delivered for introduction into interstate commerce that is not in compliance with this section is subject to regulatory action.

§ 310.545 [Amended]

3. Section 310.545 *Drug products containing certain active ingredients offered over-the-counter (OTC) for certain uses* is amended by removing and reserving paragraph (a)(9), and by revising paragraph (d)(1) to read as follows:

§ 310.545 Drug products containing certain active ingredients offered over-the-counter (OTC) for certain uses.

(d) * * *

(1) May 7, 1991, for products subject to paragraphs (a)(1) through (a)(4), (a)(6)(i)(A), (a)(6)(ii)(A), (a)(7) (except as covered by paragraph (d)(3) of this section), (a)(8)(i), (a)(10)(i) through (a)(10)(iii), (a)(12)(i) through (a)(12)(iv), and (a)(14) through (a)(18)(i) of this section.

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Dated: April 13, 1995.

William K. Hubbard,

Acting Deputy Commissioner for Policy.

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