DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 333 and 448

[Docket No. 76N-482A]

RIN 0905-AA06

Topical Antimicrobial Drug Products for Over-the-Counter Human Use; Proposed Amendment of Final Monograph for OTC First Aid Antibiotic Drug Products

AGENCY: Food and Drug Administration.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a notice of proposed rulemaking that would amend the final monograph for over-the-counter (OTC) first aid antibiotic drug products in 21 CFR part 333 that establishes conditions under which these drug products are generally recognized as safe and effective and not misbranded. The amendment would revise the standards for bacitracin zinc-polymyxin B sulfate topical aerosol. FDA is concurrently amending the antibiotic regulations in 21 CFR part 448 to be consistent with the monograph for OTC first aid antibiotic drug products. This proposal is a part of the ongoing review of OTC drug products conducted by FDA.

DATES: Written comments by July 10, 1990. Requests for an informal conference on proposed change in § 448.513e(a)(1) by June 11, 1990.

ADDRESSES: Written comments or request for conference on proposed change in § 448.513e to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 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 December 11, 1987 (52 FR 47312), FDA issued a final monograph for OTC first aid antibiotic drug products (21 CFR part 333, subpart B). The monograph provides for bacitracin zinc-polymyxin B sulfate topical aerosol containing, in each 90-gram container, 10,000 units of bacitracin and 200,000 units of polymyxin B (§ 333.120(a)(7)) (21 CFR 333.120(a)(7)).

On June 3, 1988, FDA received a citizen petition (Docket No. 76N-0482/CP) requesting the amendment of § 333.120(a)(7) to delete the "90-gram" specification for the container size so that § 333.120(a)(7) would be consistent with the antibiotic regulation in § 448.513e(a)(1) which does not specify a container size for bacitracin zinc-polymyxin B sulfate topical aerosol.

On October 13, 1989, FDA received an amendment to the citizen petition (Docket No. 76N-0482/AMD1) requesting that § 333.120(a)(7) be revised to state the concentration of antibiotics contained in each gram, rather than the current designation of the concentration of antibiotics contained in each "90-gram" container. The petitioner stated that vehicles and/or inert gases that could be used in the aerosol product vary in specific gravity and/or weight. The petitioner mentioned that if it wished to reformulate the product to change, add, or delete either the "suitable vehicle" or the "suitable inert gases," the final product would still provide the same number of units of antibiotics but the total container content might be at variance from the required 90 grams. Accordingly, the petitioner requested that § 333.120(a)(7) be revised to read "Bacitracin zinc-polymyxin B sulfate topical aerosol containing, in each gram, 120 units of bacitracin zinc and 2,350 units of polymyxin B * * *." The petitioner concluded that this approach would be consistent with other monograph listings in §§ 333.110 and 333.120.

In developing the final monograph for OTC first aid antibiotic drug products, the agency stated that the dosage forms included in the monograph reflect those dosage forms currently identified in subpart F of the specific antibiotic regulations that apply to first aid antibiotics (52 FR 47312 at 47313). Although § 448.513e does not state a container size, as the petitioner noted, that particular section of the antibiotic regulations was based on an approved new drug application (NDA) for an aerosol product in a 90-gram container. When the final monograph for OTC first aid antibiotic drug products was prepared, it was necessary to state therein the size of the container to inform other manufacturers of the amount of antibiotics per total container size. After publication of the final monograph for OTC first aid antibiotic drug products, the agency was notified that the underlying NDA for the aerosol product had been amended to provide for a change in the container size from a 90-gram container to an 85-gram container, as allowed under § 314.70(d) (21 CFR 314.70(d)). The amount of antibiotics per 85-gram container remained the same in accord with § 448.513e(a)(1): 10,000 units of bacitracin and 200,000 units of polymyxin B. These amounts are equivalent to 117.65 units of bacitracin per gram and 2352.94 units of polymyxin B per gram, and are very close to the rounded-off amounts requested by the petitioner.

After reviewing the citizen petition, the agency agrees that it would be appropriate to revise §§ 333.120(a)(7) and 448.513e(a)(1) to state the concentration of antibiotics contained in each gram of the final product. This proposed amendment would allow manufacturers to market other size aerosol products containing these antibiotics and would allow greater flexibility in reformulating existing products if the manufacturer elected to change the suitable vehicle and/or inert gases. Therefore, the agency is proposing to amend the final monograph for OTC first aid antibiotic drug products in § 333.120(a)(7) and the existing antibiotic regulation in § 448.513e(a)(1) to provide for bacitracin zinc-polymyxin B sulfate topical aerosol containing, in each gram, 120 units of bacitracin and 2,350 units of polymyxin B. In addition, the agency is correcting an error that currently exists in § 448.513e(a)(1): 120 percent should read 130 percent.

The agency advises that any final rule resulting from this proposed rule will be effective 12 months after its date of publication in the **Federal Register**. On or after that date, any OTC drug product that is not in compliance may not be initially introduced or initially delivered for introduction into interstate commerce unless it is the subject of an approved application. Further, any OTC drug product subject to the rule that is repackaged or relabeled after the effective date of the rule must be in compliance with the rule regardless of the date the product was initially introduced into interstate commerce. Manufacturers are encouraged to comply voluntarily with the rule at the earliest possible date.

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 first aid antibiotic 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 first aid antibiotic drug products is not expected to pose such an effect 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 first aid antibiotic drug products. Comments regarding the impact of this rulemaking on OTC first aid antibiotic 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 July 10, 1990, submit to the Dockets Management Branch (address above) written comments regarding this proposal. Three copies of all comments are to be submitted except that individuals may submit one copy. Comments 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 may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Interested persons may, on or before June 11, 1990, submit to the Dockets Management Branch a request for an informal conference on the proposed change in § 448.513e(a)(1). The participants in an informal conference, if one is held, will have until July 10, 1990, or 30 days after the date of the conference, whichever is later, to submit their comments.

List of Subjects in

21 CFR Part 333

First aid antibiotic drug products, Labeling, Over-the-counter drugs.

21 CFR Part 448

Antibiotics.

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 parts 333 and 448 as follows:

PART 333—TOPICAL ANTIMICROBIAL DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

1. The authority citation for 21 CFR part 333 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 333.120 is amended by revising paragraph (a)(7) to read as follows:

§ 333.120 Permitted combinations of active ingredients.

* * * * *

(a) * * *

(7) Bacitracin zinc-polymyxin B sulfate topical aerosol containing, in each gram, 120 units of bacitracin and 2,350 units of polymyxin B in a suitable vehicle, packaged in a pressurized container with suitable inert gases: *Provided*, That it meets the tests and methods of assay in § 448.513e(b) of this chapter.

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PART 448—PEPTIDE ANTIBIOTIC DRUGS

3. The authority citation for 21 CFR part 448 continues to read as follows:

Authority: Sec. 507 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 357).

4. Section 448.513e is amended by revising paragraph (a)(1) to read as follows:

§ 448.513e Bacitracin zinc-polymyxin B sulfate topical aerosol.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Bacitracin zinc-polymyxin B sulfate topical aerosol is bacitracin zinc, polymyxin B sulfate in a suitable and harmless vehicle, packaged in a pressurized container with suitable and harmless inert gases. Each gram contains 120 units of bacitracin and 2,350 units of polymyxin B. Its bacitracin content is satisfactory if it is not less than 90 percent and not more than 130 percent of the number of units of bacitracin that it is represented to contain. Its polymyxin B content is satisfactory if it is not less than 90 percent and not more than 130 percent of the number of units of polymyxin B that it is represented to contain. Its moisture content is not more than 0.5 percent. It contains not more than an average of 10 microorganisms per container. The bacitracin zinc used conforms to the standards prescribed by § 448.13(a)(1). The polymyxin B sulfate used conforms to the standards prescribed by § 448.30(a)(1).

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Dated: March 27, 1990.

James S. Benson,

Acting Commissioner of Food and Drugs.

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