DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 310

[Docket No. 81N-0040]

Insect Repellent Drug Products for Over-the-Counter Oral Human Use

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule establishing conditions under which over-the-counter (OTC) insect repellent drug products for oral use (an orally administered drug product intended to keep insects away) are not generally recognized as safe and effective and are misbranded. No comments or new data were submitted in response to the agency's proposed rule. This final rule is part of the ongoing review of OTC drug products conducted by FDA.

EFFECTIVE DATE: December 17, 1985.

FOR FURTHER INFORMATION CONTACT: William 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 January 5, 1982 (47 FR 424), FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking to establish a monograph for OTC insect repellent drug products for oral use, together with the recommendations of the Advisory Review Panel on OTC Miscellaneous Internal Drug Products, which was the advisory review panel responsible for evaluating data on the active ingredients in this drug class. Interested persons were invited to submit comments by April 5, 1982. Reply comments in response to comments filed in the initial comment period could be submitted by May 5, 1982.

In accordance with § 330.10(a)(10), the data and information considered by the Panel were put on display in the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857, after deletion of a small amount of trade secret information.

The agency's proposed regulation for insect repellent drug products for oral use was published in the **Federal Register** of June 10, 1983 (48 FR 26986). Interested persons were invited to file by August 9, 1983, written objections and requests for an oral hearing before the Commission of Food and Drugs regarding the proposal. Interested persons were invited to file comments on the agency's economic impact determination by August 9, 1983. New data could have been submitted until June 11, 1984. Final agency action occurs with the publication of this final rule for OTC insect repellent drug products for oral use.

The OTC procedural regulations (21 CFR 330.10) have been revised to conform to the decision in *Cutler* v. *Kennedy,* 475 F. Supp. 838 (D.D.C. 1979). (See the **Federal Register** of September 29, 1981; 46 FR 47730.) The court in *Cutler* held that the OTC drug review regulations were unlawful to the extent that they authorized the marketing of Category III drugs after a final monograph had been established. Accordingly, this provision has been deleted from the regulations, which now provide that any testing necessary to resolve the safety or effectiveness issues that formerly resulted in a Category III classification, and submission to FDA of the results of that testing or any other data, must be done during the OTC drug rulemaking process before the establishment of a final monograph.

Although it was not required to do so under *Cutler,* FDA is no longer using 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 monograph stage, but is using instead the terms "monograph conditions" (old Category I) and "nonmonograph conditions" (old Categories II and III).

As discussed in the proposed regulation for OTC insect repellent drug products for oral use (48 FR 26986), 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 on December 17, 1985. On or after that date, no OTC drug products that are subject to the final 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 final rule at the earliest possible date

No comments, new data, or requests for oral hearing were submitted in response to the proposed rule on OTC insect repellent drug products for oral use. No additional information has come to the agency's attention since publication of the proposed rule.

The Agency's Final Conclusions on OTC Insect Repellent Drug Products for Oral Use

FDA has considered the data and information available at this time and concludes that any OTC drug product that is labeled, represented, or promoted for oral use as an insect repellent is regarded as a new drug within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321(p)) for which an approved new drug application under section 505 of the act (21 U.S.C. 355) and 21 CFR Part 314 is required for marketing. In the absence of an approved new drug application, such product is also misbranded under section 502 of the act (21 U.S.C. 352).

No comments were received in response to the agency's request for specific comment on the economic impact of this rulemaking (47 FR 424). The agency has examined the economic consequences of this final rule 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 not one of these rules, including this final rule for OTC insect repellent drug products for oral use, 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 insect repellent drug products for oral use is not expected to pose such an impact on small businesses. Therefore, the agency certifies that this final rule will not have a significant economic impact on a substantial number of small entities.

List of Subjects in 21 CFR Part 310

New drugs.

PART 310—[AMENDED]

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

Administrative Procedure Act, Subchapter D of Chapter I of Title 21 of the Code of Federal Regulations is amended in Part 310 as follows:

1. The authority citation for 21 CFR Part 310 is revised to read as follows:

Authority: Secs. 502, 503, 505, 701, 52 Stat. 1051, 1052, 1053, 1055, as amended (21 U.S.C 352, 353, 355, 371) (5 U.S.C. 553); 21 CFR 5.11.

2. In Subpart E by adding new § 310.529, to read as follows:

§ 310.529 Drug products containing active ingredients offered over-the-counter (OTC) for oral use as insect repellents.

(a) Thiamine hydrochloride (vitamin B–1) has been marketed as an ingredient in over-the-counter (OTC) drug products for oral use as an insect repellent (an orally administered drug product intended to keep insects away). There is a lack of adequate data to establish the effectiveness of this, or any other ingredient for OTC oral use as an insect repellent. Labeling claims for OTC orally administered insect repellent drug products are either false, misleading, or unsupported by scientific data. The following claims are examples of some that have been made for orally administered OTC insect repellent drug products: "Oral mosquito repellent," "mosquitos avoid you," "bugs stay away," "keep mosquitos away for 12 to 24 hours," and "the newest way to fight mosquitos." Therefore, any drug product containing ingredients offered for oral use as an insect repellent cannot be generally recognized as safe and effective.

(b) Any OTC drug product that is labeled, represented, or promoted for oral use as an insect repellent 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 FD–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 OTC as an insect repellent for oral use is safe and effective for the purpose intended.

(d) Any such drug product in interstate commerce after December 17, 1985, that is not in compliance with this section is subject to regulatory action.

Dated: May 6, 1985.

Frank E. Young,

Commissioner of Food and Drugs.

Margaret M. Heckler,

Secretary of Health and Human Services.

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