DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 358

[Docket No. 80N-0146]

Nailbiting and Thumbsucking Deterrent Drug Products for Over-the-Counter Human Use; Tentative Final Monograph

AGENCY: Food and Drug Administration.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Food and Drug Administration (FDA) is issuing a notice of proposed rulemaking in the form of a tentative final monograph that would establish conditions under which over-the-counter (OTC) nailbiting and thumbsucking deterrent drug products are generally recognized as safe and effective and not misbranded. FDA is issuing this notice of proposed rulemaking after considering the report and recommendations of the Advisory Review Panel on OTC Miscellaneous External Drug Products and the public comment 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 before the Commissioner of Food and Drugs on the proposed regulation by November 2, 1982. New data by September 3, 1983.

Comments on the new data by November 3, 1983. 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). Comments on the agency's economic impact determination by January 2, 1983.

ADDRESS: Written comments, objections, 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. New data and comments on new data should also be addressed to the Dockets Management Branch.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, National Center for Drugs and Biologics (HFD-510), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-4960.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of October 17, 1980 (45 FR 69122) 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 nailbiting and thumbsucking deterrent drug products, together with the recommendations of the Advisory Review Panel on OTC Miscellaneous External 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 January 15, 1981. Reply comments in response to comments filed in the initial comment period could be submitted by February 16, 1981.

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.

The advance notice of proposed rulemaking, which was published in the **Federal Register** on October 17, 1980 (45 FR 69122), was designated as a "proposed monograph" in order to conform to terminology used in the OTC drug review regulations (21 CFR 30.10). Similarly, the present document is designated in the OTC drug review regulations as a "tentative final monograph." Its legal status, however, is that of a proposed rule. In this tentative final monograph (proposed rule) the FDA states for the first time its position on the establishment of a monograph for OTC nailbiting and thumbsucking deterrent drug products. Final agency action on this matter will occur with the publication at a future date of a final monograph, which will be a final rule establishing a monograph for OTC nailbiting and thumbsucking deterrent drug products.

In response to the advance notice of proposed rulemaking, one consumer submitted a comment. A copy of the comment received is also on public display in the Dockets Management Branch.

This proposal would amend Subchapter D of Chapter I of Title 21 of the Code of Federal Regulations in Part 358 by adding Subpart C. This proposal constitutes FDA tentative adoption of the Panel's conclusions and recommendations on OTC nailbiting and thumbsucking deterrent drug products as modified on the basis of the comment received and the agency's independent evaluation of the Panel's report. Modifications have ben made for clarity and regulatory accuracy and are reflected in this tentative final monograph. The agency emphasizes that no nailbiting and thumbsucking deterrent active ingredients have been determined to be generally recognized as safe and effective and not misbranded. However, the agency is proposing Category I labeling in this document in the event that data are submitted which result in the upgrading of any ingredient to monograph status in the final rule.

FDA published in the **Federal Register** of September 29, 1981 (46 FR 47730) a final rule revising the OTC procedural regulations to conform to the decision in *Cutler* v. *Kennedy*, 475 F. Supp. 838 (D.D.C. 1979). The Court in *Cutler* held that the OTC drug review regulations (21 CFR 330.10) were unlawful to the extent that they authorized the marketing of Category III drugs after a final monograph had been established. Accordingly, this provision is now deleted from the regulations. The regulations 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 (46 FR 47738).

Although it was not required to do so under *Cutler*, FDA will no longer use the terms "Category I," "Category II," and "Category III" at the final monograph stage in favor of the terms "monograph conditions" (old Category I) and "nonmonograph conditions" (old Categories II and III). This document retains the concepts of Categories I, II, and III at the tentative final monograph stage.

The agency advises that the conditions under which the drug products that are subject to this monograph would be generally recongized as safe and effective and not misbranded (monograph conditions) will be effective 12 months after the date of publication of the final monograph in the **Federal Register.** On or after that date, no OTC drug products that are subject to the monograph and that contain nonmonograph conditions, i.e., conditions that would cause the drug to be not generally recognized as safe and effective or to be misbranded, may be initially introduced or initially delivered for introduction into interstate commerce unless they are the subject of an approved new drug application. Further, any OTC drug products subject to this monograph that are repackaged or relabeled after the effective date of the monograph must be in compliance with the monograph regardless of the date the product was initially introduced or initially delivered for introduction into interstate commerce. Manufactur

are encouraged to comply voluntarily with the monograph at the earliest possible date.

In the advance notice of proposed rulemaking for OTC nailbiting and thumbsucking deterrent drug products (published in the **Federal Register** of October 17, 1980 (45 FR 69122)), the agency suggested that the conditions included in the monograph (Category I) be effective 30 days after the date of publication of the final monograph in the **Federal Register** and that the conditions excluded from the monograph (Category II) be eliminated from OTC drug products effective 6 months after the date of publication of the final monograph, regardless of whether further testing was undertaken to justify their future use. Experience has shown that relabeling of products covered by the monograph is necessary in order for manufacturers to comply with the monograph. New labels containing the monograph labeling have to be written, ordered, received, and incorporated into the manufacturing process. The agency has determined that it is impractical to expect new labeling to be in effect 30 days after the date of publication of the final monograph. Experience has shown also that if the deadline for relabeling is too short, the agency is burdened with extension requests and related paperwork.

In addition, some products will have to be reformulated to comply with the monograph. Reformation often involves the need to do stability testing on the new product. An accelerated aging process may be used to test a new formulation; however, if the stability testing is not successful, and if further reformulation is required, there could be a further delay in having a new product available for manufacture.

The agency wishes to establish a reasonable period of time for relabeling and reformulation in order to avoid an unnecessary disruption of the marketplace that could not only result in economic loss, but also interfere with consumers' access to safe and effective drug products. Therefore, the agency is proposing that the final monograph be effective 12 months after the date of its publication in the **Federal Register**. The agency believes that within 12 months after the date of publication most manufacturers can order new labeling and reformulate their products and have them in compliance in the marketplace. However, if the agency determines that any labeling for a condition included in the final monograph should be implemented sooner, a shorter deadline may be established. Similarly, if a safety problem is identified for a particular nonmonograph condition, a shorter deadline may be set for removal of that condition from OTC drug products.

I. The Agency's Tentative Conclusions on the Comment

One comment questioned how the government could become involved in such a trivial matter as proposing a rule on nailbiting and thumbsucking deterrent drug products. The comment requested that the agency not issue this rule.

As part of the agency's review of all OTC drug products, the Panel considered the safety and effectiveness of many classes of OTC miscellaneous external drug products. Although nailbiting and thumbsucking deterrent drug products affect only a small group of consumers, the agency believes that all marketed OTC drug products should be both safe and effective and not misbranded for their intended use. Accordingly, the agency is continuing with this rulemaking proceeding.

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

A. Summary of Ingredient Categories and Testing of Category II and Category III Conditions

1. *Summary of ingredient categories.* The agency has reviewed the two claimed active ingredients, denatonium benzoate and sucrose octaacetate, submitted to the Panel and concurs with the Panel's categorization of these ingredients in Category III.

The Panel placed denatonium benzoate (0.35 percent or less) and sucrose octaacetate (6 percent or less) in Category III because the available data were insufficient to permit final classification. The Panel concluded that both denatonium benzoate and sucrose octaacetate are safe for adults and children 4 years of age and older, but there are insufficient data to determine their effectiveness as nailbiting and thumbsucking deterrent drug products. FDA concurs with the Panel's Category III classification of denatonium benzoate and sucrose octaacetate as single active ingredients.

The Panel recognized the combination of denatonium benzoate and sucrose octaacetate as a Category III combination because the perception of a bitter taste may vary from person to person and from ingredient to ingredient. FDA agrees with the Panel's Category III classification because there are insufficient data to establish the effectiveness of the combination.

For the convenience of the reader, the following table is included as a summary of the categorization of nailbiting and thumbsucking deterrent active ingredients:

Ingredient	Categorization
Denatonium benzoate	III.
Sucrose octaacetate	III.

2. *Testing of Category II and Category III conditions.* The Panel recommended testing guidelines for nailbiting and thumbsucking deterrent drug products (45 FR 69127). The agency is offering these guidelines as the Panel's recommendations without adopting them or making any formal comment on them. Interested persons may communicate with the agency about the submission of data and information to demonstrate the safety or effectiveness of any nailbiting and thumbsucking deterrent ingredient or condition included in the review by following the procedures outlined in the agency's policy statement published in the **Federal Register** of September 29, 1981 (46 FR 47740). This policy statement includes procedures for the submission and review of proposed protocols, agency meetings with industry or other interested persons, and agency communications on submitted test data and other information.

B. Summary of the Agency's Changes in the Panel's Recommendations

FDA has considered the comment and other relevant information and concludes that it will tentatively adopt the Panel's report and recommended monograph with the changes described in the summary below.

1. In accord with the monograph format currently being used in other tentative final monographs, the agency proposes to combine the Panel's recommended indications in § 358.250(b)(1), (2), and (3) (redesignated § 358.250(b)) to read as follows: "For use as a" (select one of the following: "nailbiting," "thumbsucking," or "nailbiting and thumbsucking") "deterrent in persons aged 4 years and older."

In addition, the agency also proposes to combine the Panel's recommended directions in § 358.250(d)(1), (2), and (3) (redesignated § 358.250(d)) to read as follows in the tentative final monograph: "Apply to the" (select one of the following: "nail," "thumb," or "nail or thumb") "after washing hands and at bedtime."

2. The Panel recommended that the directions for use in § 358.250(d) be followed by the phrase "or as directed by a physician." Believing that the word

"doctor" is more commonly used and better understood by consumers, the agency is substituting the word "doctor" for "physician" in this phrase in the tentative final monograph. If the word "doctor" is adopted in the final monograph, the agency will use this language in othere final monographs and other applicable OTC drug regulations and will propose amendments to those regulations accordingly. Public comment on this proposed change in labeling language is invited.

3. Based on a review of the labels of products submitted to the Panel, the warning in § 358.250(c)(2) has been expanded to include the terms "flammable" and "heat." The agency believes that this additional information provides a more informative warning and proposes that the warning in § 358.250(c)(2) read as follows in the tentative final monograph: "Flammable, keep away from heat or flame."

The agency has examined the economic consequences of this proposed rulemaking and has determined that it does not require either a Regulatory Impact analysis, as specified in Executive Order 12291, or a Regulatory Flexibility Analysis, as defined in the Regulatory Flexibility Act (Pub. L. 96-354). Specifically, nailbiting and thumbsucking deterrent drug products containing denatonium benzoate and sucrose octaacetate may continue to be marketed while additional testing is being performed. If neither of these ingredients is elevated to Category I status, then there will be no active ingredients to include in a final monograph, and these products will have to be removed from the market. If either of these ingredients is elevated to Category I status, some relabeling will be necesary because the agency has made some minor revisions in the Panel's recommended labeling. Manufacturers will have up to 12 months to revise their product labeling. In most cases, this will be done at the next printing so that minimal costs should be incurred. Thus, the impact of a final rule appears to be minimal whether or not the ingredients are elevated to Category I status. Therefore, the agency concludes that the proposed rule is not a major rule as defined in Executive Order 12291. Further, the agency certifies that the proposed rule, if implemented, will not have a significant economic impact on a substantial number of small entities as defined in the Regulatory Flexibility Act.

The agency invites public comment regarding any substantial or significant economic impact that this rulemaking would have on OTC nailbiting and thumbsucking deterrent drug products. Types of impact may include, but are not limited to, costs associated with product testing, relabeling, repackaging, or reformulating. Comments regarding the impact of this rulemaking on OTC nailbiting and thumbsucking deterrent drug products 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 nailbiting and thumbsucking deterrent 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 careully considered the potential environmental effects of this proposal and has concluded that the action will not have significant impact on the human environment and an environmental impact statement therefore will not be prepared. The agency's finding of no significant impact and the evidence supporting this finding, contained in an environmental assessment (under 21 CFR 25.31, proposed in the **Federal Register** of December 11, 1979; 44 FR 71742), may be seen in the Dockets Management Branch, Food and Drug Administration.

List of Subjects in 21 CFR Part 358

Over-the-counter drugs, Skin bleaching agents, Wart removers, Nailbiting and thumbsucking deterrents, Ingrown toenail relief.

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 as revised (see 47 FR 16010; April 14, 1982), it is proposed that Subchapter D of Chapter I of Title 21 of the Code of Federal Regulations be amended in Part 358 by adding new Subpart C, to read as follows:

PART 358—MISCELLANEOUS EXTERNAL DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

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Subpart C—Nailbiting and Thumbsucking Deterrent Drug Products

Sec.
358.201 Scope.
358.203 Definitions.
358.210 Nailbiting and thumbsucking deterrent active ingredients. [Reserved]
358.250 Labeling of nailbiting and thumbsucking deterrent drug products.

Authority: 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); secs. 4, 5, and 10, 60 Stat 238 and 243 as amended (5 U.S.C. 553, 554, 702, 703, 704).

Subpart C—Nailbiting and Thumbsucking Deterrent Drug Products

§ 358.201 Scope.

(a) An over-the-counter nailbiting and thumbsucking deterrent drug product in a form suitable for topical administration is generally recognized as safe and effective and is not misbranded if it meets each of the conditions in this subpart in addition to each of the general conditions established in § 330.1.

(b) References in this subpart to regulatory sections of the Code of Federal Regulations are to Chapter I of Title 21 unless otherwise noted.

§ 358.203 Definitions.

As used in this subpart:

(a) *Nailbiting.* The habitual biting of the fingernails.

(b) Thumbsucking. The habitual sucking of a thumb.

§ 358.210 Nailbiting and thumbsucking deterrent active ingredients. [Reserved]

§ 358.250 Labeling of nailbiting and thumbsucking deterrent drug products.

(a) *Statement of identity.* The labeling of the product contains the established name of the drug, if any, and identifies the product as a "nailbiting deterrent," "thumbsucking deterrent," or "nailbiting-thumbsucking deterrent."

(b) *Indications.* The labeling of the product contains a statement of the indications under the heading "Indications" that is limited to the following: "For use as a" (select one of the following: "nailbiting," "thumbsucking," or "nailbiting and thumbsucking") "deterrent in persons aged 4 years and older."

(c) *Warnings.* The labeling of the product contains the following warnings under the heading "Warnings":

(1) "Avoid contact with eyes."

(2) "For topical use only."

(3) *For products containing flammable vehicles.* "Flammable, keep away from heat or flame."

(d) *Directions.* The labeling of the product contains one of the following directions under the heading "Directions," "Apply to the" (select one

of the following: "nail," "thumb," or "nail or thumb") "after washing hands and at bedtime or as directed by a doctor."

Interested persons may, on or before November 2, 1982, 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 on the proposed regulation. A request for an oral hearing must specify points to be covered and time requested. Written comments on the agency's economic impact determination may be submitted on or before January 2, 1983. Three copies of all comments, objections, and request 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 above office 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 September 3, 1983, 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 November 3, 1983. 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 above office between 9 a.m. and 4 p.m., Monday through Friday.

In establishing a final monograph, the agency will ordinarily consider only data submitted prior to the closing of the administrative record on November 3, 1983. Data submitted after the closing of the administrative record will be reviewed by the agency only after a final monograph is published in the **Federal Register**, unless the Commissioner finds good cause has been shown that warrants earlier consideration.

Mark Novitch,

Acting Commissioner of Food and Drugs.

Dated: August 9, 1982.

Richard S. Schweiker,

Secretary of Health and Human Services.

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