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April 2, 2001

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VIA FEDERAL EXPRESS

Dockets Management Branch
Food and Drug Administration
Room 1-23
12420 Parklawn Drive
Rockville, MD 20857

Re: **Citizen Petition Requesting The Establishment Of A Final Regulation For Nailbiting And Thumbsucking Deterrent Drug Products For Over-The-Counter Human Use; Docket No. 80N-0146**

Dear Sir or Madam:

In accordance with 21 C.F.R. § 10.20(a), enclosed please find four copies of the above Citizen Petition being submitted on behalf of Oakhurst Company. This Petition requests that the Food and Drug Administration revoke the final rule on over-the-counter ("OTC") nailbiting and thumbsucking deterrent products (21 C.F.R. § 310.536), and establish a monograph under the section reserved for nailbiting and thumbsucking drug products (21 C.F.R. pt. 358) by declaring that an OTC nailbiting and thumbsucking deterrent product in a form suitable for topical administration is generally recognized as safe and effective and is not misbranded if it contains cayenne pepper or denatonium benzoate.

Please do not hesitate to contact us if you have any questions or comments in this regard. Thank you in advance for your prompt attention to this matter.

Sincerely,

Gary L. Yingling

GLY/mhh
Enclosure(s)
cc: Oakhurst Company

CP4

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Re: **Citizen Petition Requesting The Establishment Of A Final Regulation For Nailbiting And Thumbsucking Deterrent Drug Products For Over-The-Counter Human Use; Docket No. 80N-0146**

Dear Sir or Madam:

The undersigned submits this Citizen Petition ("Petition") on behalf of petitioner Oakhurst Company, 3000 Hempstead Turnpike, Levittown, New York ("Oakhurst"), to request the establishment of a final regulation for nailbiting and thumbsucking deterrent products for over-the-counter ("OTC") human use, and the revocation of the "negative" regulation that currently encompasses these drug products. 58 Fed. Reg. 46,749 (Sept. 2, 1993) (codified at 21 C.F.R. § 310.536).

Oakhurst owns the manufacturing and distribution rights to an aversive taste therapy product called THUM® that contains cayenne pepper[1/] and has been marketed to help deter persons from nailbiting and thumbsucking since 1935.[2/]

1/ Also known as "capsicum." See The Pharmacopeia of the United States of America 105 (11th Decennial rev., 1936).

2/ See Exhibit 1: U.S. Patent Office Statement, Certificate of Trademark Renewal.

Additionally, Oakhurst is considering marketing an aversive taste therapy product containing denatonium benzoate as an active ingredient. The petitioner has included statements from medical and scientific experts in the use of aversive taste therapy as well as references to scientific studies demonstrating the effectiveness of aversive taste therapy products such as THUM® (cayenne pepper) and a previously marketed denatonium benzoate containing product known as "Stopzit."

This Petition is being submitted under section 553(e) of the Administrative Procedures Act, 5 U.S.C. § 553(e), section 701(e) of the Federal Food, Drug, and Cosmetic Act ("the Act" or "FFDCA"), 21 U.S.C. § 371, and the implementing regulations of the Act, 21 C.F.R. §§ 10.25, 10.30 and 330.10(a)(12)(i). For the reasons discussed below, this Citizen Petition requests that the Commissioner of Food and Drugs recognize that cayenne pepper and denatonium benzoate are safe and effective ingredients for use in aversive taste therapy products used to deter nailbiting and thumbsucking.

I. ACTION REQUESTED

Oakhurst requests, under 21 C.F.R. § 330.10(a)(12)(i), that the Food and Drug Administration ("FDA") revoke the final rule on OTC nailbiting and thumbsucking deterrent products, codified at 21 C.F.R. § 310.536, and recognize that cayenne pepper and denatonium benzoate are safe and effective ingredients for use in aversive taste therapy products, as shown by peer-reviewed articles on nailbiting and thumbsucking, scientific data, and statements by experts qualified by training and experience to comment on child habit disorders and the effectiveness of products like THUM® and Stopzit. FDA may address this matter in any of the following ways:

(1) Complete the establishment of a monograph under the section reserved for nailbiting and thumbsucking deterrent products in the Tentative Final Monograph ("TFM"), 47 Fed. Reg. 39,096, 39,098 (Sept. 3, 1982) (21 C.F.R. pt. 358, subpt. C), by declaring that an OTC nailbiting and thumbsucking deterrent product in a form suitable for topical administration is generally recognized as safe and effective and is not misbranded if it contains cayenne pepper or denatonium benzoate. A proposed nailbiting and thumbsucking deterrent OTC drug product regulation is set forth at Appendix A;

(2) Recognize that the THUM® is an "old drug" and therefore outside the OTC review process; and/or

(3) Recognize that aversive taste treatment products containing safe ingredients are cosmetics that fall outside the OTC review process.

II. STATEMENT OF GROUNDS

On September 2, 1993, the FDA published a final rule declaring that any OTC drug product containing ingredients offered for use as nailbiting or thumbsucking deterrent products cannot be generally recognized as safe and effective. See 58 Fed. Reg. 46,749. The final rule states that any OTC drug product that is labeled, represented, and promoted as a nailbiting or thumbsucking deterrent will be regarded as a new drug within the meaning of section 201(p) of the Act. The final rule references "cayenne pepper" and "denatonium benzoate" as examples of ingredients for which there is a lack of adequate data to establish general recognition of safety and effectiveness. 58 Fed. Reg. at 46,754, (codified at 21 C.F.R. § 310.536(a)).

A. Cayenne Pepper

1. Cayenne Pepper Is A Safe And Effective Ingredient In Products Such As THUM® Which Are Used To Deter Nailbiting and Thumbsucking

Cayenne pepper is an ingredient that FDA lists in its food regulations as a "generally recognized as safe" spice, natural seasoning and flavoring. 21 C.F.R. § 182.10. It is a natural ingredient that has been used safely and effectively in THUM® for sixty-five years. THUM®, and products like THUM®, should not be removed from the market by administrative fiat simply because FDA failed to adequately review the published literature and scientific data documenting the safety and effectiveness of aversive taste therapy products. Even a cursory review of the articles in peer-reviewed journals shows that medical experts in pediatrics, dentistry, and psychology agree that nailbiting and thumbsucking are habits that may be successfully treated with aversive taste therapy products such as THUM®. Furthermore, we submit data from numerous studies on nailbiters and thumbsuckers that document that these products have a significant effect over time. These studies, often conducted with grants by NIH and/or HHS, detail their methods of randomization, control and test conditions, and analytical methods and

constitute substantial scientific evidence that aversive taste therapy products such as THUM® are safe and effective when used to deter nailbiting and thumbsucking.

Because controlled studies show that aversive taste therapy products such as THUM® are safe and effective treatments for nailbiting and thumbsucking, Oakhurst requests, in accordance with 21 C.F.R. § 330.10(a)(12)(i), that FDA revoke section 310.536 and concurrently issue a regulation under the section reserved for nailbiting and thumbsucking deterrent products, 21 C.F.R. pt. 358, subpt. C, declaring that an OTC nailbiting and thumbsucking deterrent product in a form suitable for topical administration is generally recognized as safe and effective and is not misbranded if it contains cayenne pepper.

According to 21 C.F.R. § 330.10(a)(4)(i), an OTC drug ingredient will be judged safe if it has:

> [A] low incidence of adverse reactions or significant side effects under adequate directions for use and warnings against unsafe use as well as a low potential for harm which may result from abuse under conditions of widespread availability. Proof of safety shall consist of adequate tests by methods reasonably applicable to show the drug is safe under the prescribed, recommended, or suggested conditions of use. This proof shall include results of significant human experience during marketing. General recognition of safety shall ordinarily be based upon published studies which may be corroborated by unpublished studies and other data.

Similarly, the effectiveness of an OTC drug ingredient will be judged on the basis of:

> [A] reasonable expectation that, in a significant proportion of the target population, the pharmacological effect of the drug, when used under adequate directions for use and warnings against unsafe use, will provide clinically significant relief of the type claimed. Proof of effectiveness shall consist of controlled clinical investigations as defined in § 314.126(b) . . . unless this

> requirement is waived on the basis of a showing that it is not reasonably applicable to the drug or essential to the validity of the investigation and that an alternative method of investigation is adequate to substantiate effectiveness. Investigations may be corroborated by partially controlled or uncontrolled studies, documented clinical studies by qualified experts, and reports of significant human experience during marketing. . . . General recognition of effectiveness shall ordinarily be based upon published studies which may be corroborated by unpublished studies and other data.

21 C.F.R. § 330.10(a)(4)(ii).

To demonstrate that cayenne pepper is safe and effective when used in nailbiting and thumbsucking deterrent products, petitioner submits the following: (1) The THUM® product contains cayenne pepper extract and has been marketed as a safe and effective aversive therapy product for nailbiting and thumbsucking for sixty-five years; (2) Adequate scientific evidence exists that aversive taste therapy products such as THUM® are safe and effective; (3) Aversive taste therapy products such as THUM® are commonly recommended treatments for nailbiting and thumbsucking; and (4) Aversive taste therapy products such as THUM® are appropriate for OTC drug rulemaking because the conditions are readily recognizable and the benefits derived from the use of these products outweigh any risks associated with their OTC availability. Oakhurst is specifically including data and information regarding the effectiveness of aversive taste therapy in response to FDA's comment in the final rule that "[n]o attempt was made to determine the effectiveness of 'aversion therapy' in changing the subjects' behavior after the drug was no longer being given." See 58 Fed. Reg. at 46,752.

Because the agency's concerns regarding the use of cayenne pepper are not supported by the weight of scientific literature and cayenne pepper has been safely included in thumbsucking and nailbiting deterrent products for sixty-five years, FDA should allow the continued marketing of thumbsucking and nailbiting deterrent products containing cayenne pepper under the regulation established for this purpose, i.e., 21 C.F.R. pt. 358, subpt. C. Past agency practice shows that the submission of additional data is not required for the agency to "up-classify" an ingredient. For example, the agency proposed the up-classification of sodium perborate monohydrate as an oral health debriding agent from Category II to

Category I in response to comments stating that the Panel did not thoroughly evaluate the available data and that a review of the Panel's report did not justify a Category II classification. 53 Fed. Reg. 2436, 2446 (Jan. 27, 1988). Similarly, the agency proposed the up-classification of aluminum sulfate as an OTC astringent ingredient in styptic pencils from Category III to Category I on the basis of a review of the Panel's recommendations and information contained in the submissions. 54 Fed. Reg. 13,490, 13,493 (Apr. 3, 1989).

(a) THUM® Has Been Marketed For Sixty-Five Years As A Safe And Effective Aversive Taste Therapy Product

The THUM® product contains cayenne pepper extract as an ingredient and has been marketed as a nailbiting and thumbsucking deterrent product continuously since 1935. Oakhurst estimates that over 8,000,000 bottles of THUM® have been sold since 1935. This marketing history is a testament to consumer acceptance of the product's safety and effectiveness. The company has sold over 300,000 bottles over the last year and has not received any complaints. The intense bitter taste of the principal ingredient, cayenne pepper, makes nailbiting and thumbsucking unpleasant. This effect, as well as consumer acceptance, marketing experience, and the controlled studies done on aversive taste therapy (see discussion below), make it clear that there is sufficient evidence under 21 C.F.R. § 330.10(a)(4) to classify cayenne pepper as a safe and effective ingredient in nailbiting and thumbsucking deterrent products.

(b) Adequate Scientific Evidence Exists To Establish That Aversive Taste Therapy Products Such As THUM® Are Safe And Effective

Petitioner submits, at Exhibit 2, the declaration of Patrick C. Friman, Ph.D., Assistant Professor of Psychology at University of Nevada, Reno. Dr. Friman received his masters and doctorate at the University of Kansas in Human Development and Developmental and Child Psychology and his bachelor's degree in Psychology at the University of Montana. Dr. Friman was a Postdoctoral fellow in Pediatric Psychology and Behavioral Pediatrics at the Department of Pediatrics, University of Kansas Medical Center.

Prior to assuming his current position at the University of Nevada, Reno, Dr. Friman held the following positions, among others: Director of Clinical Research at Boys Town; Instructor in Medical Psychology, Department of Psychiatry and Behavioral Sciences at Johns Hopkins University School of Medicine; Staff

Psychologist for Project HEALTH at the Kennedy Institute for Handicapped Children; Graduate Faculty Fellow at the University of Nebraska; Assistant Professor of Psychology in Pediatrics at the University of Pennsylvania School of Medicine; and Associate Professor in the Department of Human Communications and Otolaryngology at Creighton University School of Medicine. See curriculum vitae attached at Exhibit 2, Attachment A, for a full listing of Dr. Friman's training and professional experience.

Dr. Friman is a recognized expert in the field of pediatric psychology. He has written over fifty-seven journal articles and six books or book chapters on issues relating to child habit disorders, parent training, and medical compliance, and has one of the largest, if not the largest, individual corpus of work on thumbsucking in the United States. See Exhibit 2. Specifically, Dr. Friman has conducted (and subsequently written and/or published articles on) fifteen peer-reviewed studies on thumbsucking, five of which employed aversive taste therapy products.

We attach, for the record, the following five articles that Dr. Friman authored on aversive therapy that specifically involved the controlled experimental analysis of aversive taste therapy products as a treatment for thumbsucking behavior.

(1) Friman, P.C. and Leibowitz, J.M. "An Effective and Acceptable Treatment Alternative for Chronic Thumb- and Finger-Sucking," J. Pediatric Psychol. 15:57-65 (1990). - This study experimentally evaluated the effectiveness of aversive taste treatment for chronic thumb and finger-sucking in a randomized clinical trial. The results showed substantial reductions in chronic thumbsucking with continued high rates of cessation after three months and one year. The study included twenty-two children ages four through eleven who were randomly assigned to either treatment or control groups.

(2) Friman, P.C., Barone, V.J., and Christophersen, E.R. "Aversive Taste Treatment of Finger and Thumbsucking," Pediatrics. 78:174-176 (1986). - This study experimentally evaluated the effectiveness of the contingent application of bitter fluids to the fingers or thumb of seven children who had been chronically thumbsucking since infancy. The study demonstrated that the contingent application of bitter-tasting fluids resulted in the complete elimination of thumb and finger sucking for all seven children in the study. A multiple baseline design across children and a withdrawal design were used as controls (i.e., the frequency of the behavior increased after the abrupt withdrawal of treatment and decreased after the reintroduction of the

treatment). Zero rates of thumbsucking were maintained at the three and six month follow-up for all seven children.

(3) Friman, P.C. and Hove, G. "Apparent Covariation Between Child Habit Disorders: Effects of Successful Treatment for Thumb Sucking on Untargeted Chronic Hair Pulling," J. Appl. Behav. Anal. 20:421-25 (1987). - This study experimentally evaluated the effectiveness of aversive taste treatment of thumbsucking on two children who chronically pulled their hair and sucked their thumbs. The study demonstrated that the application of bitter fluids to the thumbs of chronic thumbsuckers successfully treated their thumbsucking and eliminated the covariant hair pulling behavior. A combination of withdrawal and nonconcurrent multiple baseline designs were used as controls. Complete suppression of both behaviors was achieved through the one year follow-up.

(4) Friman, P. C. "What Would Linus Do With His blanket if His Thumb-sucking Were Treated?" Amer. J of Diseases of Children. 144:1316-1318 (1990). - This study, using a multiple baseline design, demonstrated that aversive taste treatment eliminated thumbsucking in eight thumbsucking children with concurrent attachment and that seven of the children subsequently lost interest in their attachment object. Thumbsucking levels were reduced to zero in all of the children and maintained at the zero levels at the three and six month follow-up; the initial high levels of object attachment were also reduced to zero levels in seven of the eight children during the study and follow-up period.

(5) Altman, K., Grahs, C., and Friman, P.C. "Treatment of Unobserved Trichotillomania by Attention-Reflection and Punishment of an Apparent Covariant," J. Behav. Ther. & Exp. Psychiat. 13:337-340 (1982). - This study assessed the effectiveness of aversive taste treatment of thumbsucking on untreated chronic hair pulling in a three year old girl. The study demonstrated that clinically significant decreases in hair pulling directly followed the application of a treatment which combined daily attention-reflection sessions with the application of bitter fluids to the thumb upon thumbsucking behavior. The use of a reversal design demonstrated that attention-reflection supplemented with the application of an aversive substance to treat the contingent thumbsucking behavior brought hair pulling activity to near-zero levels. No hairpulling was observed during the seventeen week follow-up period and only two occurrences were observed over an additional twenty month period.

See Exhibit 3.

Additionally, Dr. Friman recently completed yet another study which again demonstrates the effectiveness of aversive taste therapy products for the modification of the thumbsucking habit. The controlled study evaluated the effects of three different forms of thumbsucking treatment: (1) aversive taste products alone; (2) rewards alone; and (3) aversive taste products with rewards. A summary of Dr. Friman's study is attached as Attachment B to Exhibit 2 of this Petition. Although the study has not yet been published, Dr. Friman intends to submit the study to the journal Pediatrics.

Dr. Friman's controlled study used the Stopzit brand product as the aversive taste therapy agent. Although the Stopzit product contains denatonium benzoate instead of cayenne pepper, the results of the study are nevertheless relevant to all aversive taste therapy ingredients. The study was designed to demonstrate the effectiveness of aversive taste products generally, while demonstrating the specific effectiveness of a particular substance (i.e., denatonium benzoate). See discussion on denatonium benzoate at Section II.B., below. In fact, Dr. Friman has stated that any bitter substance could be used for aversive taste therapy provided that it is formulated in a product that is viscous enough to stick to the thumb and provides a sufficiently bitter taste. See Exhibit 2, Attachment B.

Thirty-six children were enrolled in the study, nine in each of the three treatment groups (i.e., aversive taste product, reward, and combined treatment (aversive taste and reward)), and nine in the control (no treatment) group. The mean age in each group was approximately 7 years. The study results indicated that all three treatment methods produced significant and substantial reductions in finger sucking when compared to the control group. Follow up observations demonstrated significant reductions continued after three months for the aversive taste product and the combined treatments. The parents of the "rewards alone" group, however, expressed less satisfaction with the treatment than the parents using the aversive taste product alone or the combined (aversive taste product / rewards) treatment. The parents using the rewards alone treatment generally questioned whether their children had actually quit sucking their fingers. Rather, the parents thought that the children had merely gotten better at hiding their habit. See id.

Dr. Friman's conclusion from this latest study is that aversive taste therapy products are very effective for the reduction and/or elimination of the thumbsucking habit. In fact, Dr. Friman has concluded that aversive taste therapy products are

"perhaps the most effective treatment currently available for finger sucking." See id.

The above referenced studies provide data, not simply anecdotal clinical experience, demonstrating that aversive taste therapy products such as THUM® successfully treat chronic thumbsuckers.[3/] The studies show a significant effect over time, identify the control and test conditions, and use a consistent experimental design.

We also attach the following two studies that involved the controlled experimental analysis of aversive taste therapy for nailbiting.[4/]

(1) Vargas, J.M. and Adesso, V.J. "A Comparison of Aversion Therapies for Nailbiting Behavior," Behav. Ther. 7:322-329 (1976). This study experimentally compared the relative effectiveness of three alternative modes of aversion therapy in modifying the behavior of chronic nailbiters. Thirty-one males and thirty females were randomly assigned to one of four groups: shock, negative practice (i.e., the nailbiting activity was actively encouraged for an uninterrupted period of time), bitter substance,[5/] and attention-

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3/ The results of these studies may be extrapolated to nailbiting behavior. As FDA noted in its response to Comment No. C00005, Docket No. 80N-0146, the finger is in the mouth longer during thumbsucking than is the finger in nailbiting, therefore giving the individual opportunity to develop a tolerance to the bitter taste. Letter to Peter S. Reichertz, Esq., Arent, Fox, Kinter & Kahn, from William E. Gilbertson, OTC Drug Evaluation (June 5, 1991). Because Dr. Friman's studies demonstrate that tolerance does not occur in the thumbsucking population, we conclude that aversive taste therapy would be equally, if not more, successful in the nailbiter population.

4/ We also explicitly incorporate by reference the four volume submission of Del Laboratories on August 31, 1983 (Docket No. 80N-0146, Comment No. C00005) which includes three clinical studies showing the effectiveness of aversive taste therapy in a patient population of nailbiters.

5/ The product used in this study was THUM®.

placebo control. All subjects completed a nailbiting questionnaire and the individual lengths of each nail was measured pre- and post-treatment to yield a composite nail-length measure for each subject. The study found that, compared to the control group, a significantly greater proportion of subjects in each of the three aversion treatment conditions had either ceased biting their nails or were biting less frequently and that this result persisted at the three month follow-up.

(2) Silber, K.P. and Haynes C.E. "Treating Nailbiting: A Comparative Analysis of Mild Aversion and Competing Response Therapies," Behav. Res. Ther. 30:15-22 (1992). This study experimentally evaluated the effectiveness of the application of a bitter substance to the nails as compared to competing response therapies and a control condition. Twenty-one subjects participated in the study, pre- and post-treatment nail measurements were obtained for each nail, and the nails were photographed. The study demonstrated that both aversive taste and competing response therapies result in significant improvement in nail length.

See Exhibit 4.

Further evidence that the active ingredients used in aversive taste therapy products such as THUM® have been studied and found to be safe, effective, and recommended treatments for thumbsucking and nailbiting is attached at Exhibit 5. On the basis of these articles and ten years of study, it is Dr. Friman's opinion that "aversive therapy products such as those employing cayenne pepper (e.g., THUM®) are successful in treating thumb-sucking and nail-biting behavior when used as instructed and, based upon the published medical literature on the subject, are generally recognized as safe and effective." See Friman declaration, Exhibit 2, Attachment C, ¶ 7.

We believe that had FDA reviewed the medical literature regarding aversive taste therapy, it would have concluded that products containing cayenne pepper, such as THUM®, are safe and effective for use as nailbiting and thumbsucking deterrents.[6/]

6/ We note that most of the data-based studies on this subject were published after 1986, several years after the report and recommendations of the Advisory

(Footnote cont'd on next page.)

(c) Aversive Taste Therapy Products Such As THUM® Are Commonly Recommended Treatments For Nailbiting And Thumbsucking

We submit, at Exhibit 6, the certificate of Barton D. Schmitt, M.D., a well-recognized expert in the field of pediatric medicine. Dr. Schmitt received his medical degree from Cornell University Medical Center and his bachelor's degree from Yale University in chemical engineering . He completed his residency in pediatrics at the University of Minnesota Hospital and a fellowship in psychosomatic aspects of pediatrics at the University of Colorado.

Dr. Schmitt is a board certified pediatrician at the Childrens' Hospital of Denver and has been a professor of pediatrics at the University of Colorado Health Sciences Center since 1975. Dr. Schmitt has participated in numerous national presentations and workshops concerning childrens' health issues and has been a member of several national committees including the American Academy of Pediatrics, Child Abuse and Neglect Task Force and the Pediatrics Review and Education Program Task Force. See curriculum vitae attached at Exhibit 6 for a full listing of Dr. Schmitt's presentations, workshops, and lectureships.

Dr. Schmitt has also written over twenty-five articles on pediatric issues in peer-reviewed journals including an article on thumbsucking and aversive taste therapy products entitled, "Thumbsucking: Pediatricians' Guidelines." Additionally, Dr. Schmitt has written over sixty-nine books, textbook articles, chapters or monographs on the subject of childrens' health, including the book, "Your Child's Health: A Pediatric Guide for Parents," which is in its second edition.

Dr. Schmitt certifies, "on the basis of twenty-nine (29) years of medical practice, that aversive taste therapy products, such as those employing cayenne pepper (e.g. THUM®), are successful in treating thumb-sucking and nail-biting behavior when used as instructed and, based upon the published medical literature

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(Footnote cont'd from previous page.)

Review Panel on OTC Miscellaneous External Drug Product ("Panel report") and TFM were issued. See 45 Fed. Reg. 69, 122 (Oct. 17, 1980) Advanced Notice of Proposed Rulemaking ("ANPR") and 47 Fed. Reg. 39,096 ("TFM") (Sept. 3, 1982).

on the subject, are generally recognized as safe and effective." Schmitt certificate Exhibit 6, ¶ 7. Additionally, both Drs. Friman and Schmitt state that they, and many of their colleagues, have in the past, and will continue to, recommend aversive taste therapy products such as THUM® to patients that have a nailbiting or thumbsucking problem. See Exhibit 2, Attachment C, ¶ 9 and Exhibit 6, ¶ 8.

A review of the published literature on nailbiting and thumbsucking as well as the articles in the popular press quickly shows that the positions articulated by Drs. Friman and Schmitt are in the medical and scientific mainstream. For example, other experts such as Dr. Edward R. Christophersen Chief of Behavioral Pediatrics at Childrens' Mercy Hospital in Kansas City, Missouri and author of "Little People: Guidelines for Common Sense Child Rearing," have espoused the use of bitter solutions in eliminating the nailbiting and thumbsucking habits in such highly visible media as Parenting (March 1993 and October 1990), Child (June/July 1991) and the New York Times (Sept. 3, 1993). See articles attached at Exhibit 7. Therefore, FDA should recognize the common sense to the position that aversive taste therapy products containing cayenne pepper are safe and effective and should remain available as OTC products.

(d) Aversive Taste Therapy Products Such As THUM® Are Appropriate For OTC Drug Rulemaking

Aversive taste therapy products such as THUM® are popular and widely recommended treatments for nailbiting and thumbsucking and are appropriate products for OTC drug rulemaking. The thumbsucking and nailbiting habits are readily recognizable, the treatments are easily applied by the individual or parent, and the benefits derived from the use of these treatments far outweigh any risks associated with their OTC availability.

The numerous articles appearing regularly in the popular press about nailbiting and thumbsucking attest to the popular interest in the subject, the pervasiveness of the habits, and the need for an OTC mode of treatment. See Exhibit 8 for a partial listing. Furthermore, it is clear from these articles that nailbiting and thumbsucking are viewed by experts qualified by training and experience to be habits and not diseases. For example, Both Drs. Friman and Schmitt have explicitly stated that "thumb-sucking and nail-biting are 'habits' and not physiological diseases." See Exhibit 2, Attachment C, ¶ 5; and Exhibit 6, ¶ 5. Similarly, Dr. Christophersen has stated in numerous interviews that "Nailbiting is just an unpleasant habit. Some of us bite our nails. Some of us twirl a pen as we talk. Some of us pull out strands of hair. Some play with paper clips." See, e.g.,

Kansas City Star, "Relax, Parents: Nailbiting is Common in Children," (July 10, 1988); Joliet (Ill) Herald-News, "Nailbiting: A Handy Guide to Help Kids Deal with the Habit," (Mar. 20, 1988)).[7/] See Exhibit 9.

In the preamble to the final rule on nailbiting and thumbsucking deterrent products, FDA suggested that thumbsucking and nailbiting could manifest themselves as "clinically significant problems." 58 Fed. Reg. at 46,750 (quoting the Oct. 17, 1980 ANPR). Petitioner has noted in Section II.C.(1) of this petition that any habit can have a more serious underlying etiology or result in a more serious condition. The point made by the scientific literature and the experts is that for many, thumbsucking and nailbiting are "empty habits" for which aversive therapies can be successful.[8/] OTC products are intended to be a first line of therapy for conditions that may be treated without medical intervention. For example, OTC digestive aids may be successfully used for gas and stomach pains. However, such products will be unsuccessful in certain medical circumstances where the stomach pain is merely a manifestation of a more serious condition such as an ulcer or stomach cancer. In the past, the agency has correctly evaluated OTC products on the basis of their effectiveness in treating conditions that are self-diagnosable and amenable to lay treatment. Petitioner notes that nailbiting and thumbsucking deterrent products containing cayenne pepper meet this standard.

The published literature on nailbiting and thumbsucking recognizes that there are some habits which, if left untreated, could result in serious medical conditions. However, the literature shows that current medical thinking of pediatricians, dentists and psychologists places these risks along a continuum where the more significant risks manifest themselves in the more severe habits. As indicated in the proposed labeling at Appendix A, nailbiting and thumbsucking deterrent products containing cayenne pepper are not labeled to address the severe habit requiring medical intervention. Instead, petitioner proposes the following caution: "Consult a physician if, after seven (7) days, there is no change in the (select one of the following: "nailbiting," "thumbsucking," "nailbiting and

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7/ See further discussion regarding the characterization of nailbiting and thumbsucking as habits, and not diseases, at Section II.C.(1).

8/ See supra n. 29.

thumbsucking") habit(s) or if the (select one of the following: "nailbiting," "thumbsucking," "nailbiting and thumbsucking") habit(s) appear(s) to increase." This caution, similar to that found on almost all OTC products, makes it clear that not all nailbiting and thumbsucking can be addressed with aversive therapy.

Therefore, FDA should create a monograph establishing that cayenne pepper is a safe and effective ingredient for use in OTC nailbiting and thumbsucking deterrent products. Both Drs. Friman and Schmitt have certified that it is their expert opinion that if commercially marketed aversive taste therapy products are no longer available, the harm that would result could be even more significant and widespread: "[I]nstead of using a safe and effective product, the consumer, normally the parent, will be required to rely on home mixtures which in all probability will not be as effective and often times will be unsafe." See Exhibit 2 and Exhibit 6. To remove from the market a properly labeled, safe and effective aversive taste therapy product containing the active ingredient cayenne pepper after sixty-five (65) years of safe and effective use is medically indefensible. Id.

2. The Ingredient Cayenne Pepper Was Not Properly Reviewed Prior To The Final Regulation For OTC Nailbiting And Thumbsucking Deterrent Products And Therefore Is Outside the Monograph

Cayenne pepper was not adequately considered in the OTC Drug Review. As will be shown below, (1) Cayenne was not reviewed by the Advisory Panel as an active ingredient of OTC nailbiting or thumbsucking deterrent products, and (2) FDA violated the Administrative Procedure Act ("APA") and its own administrative procedures by including cayenne pepper in the final rule for nailbiting and thumbsucking deterrent products. Accordingly, cayenne pepper was improperly bootstrapped into the final "negative" regulation for OTC nailbiting and thumbsucking deterrent products. Therefore, we respectfully request that the agency revoke 21 C.F.R. § 310.536 and establish a "positive" monograph for OTC nailbiting and thumbsucking deterrent drug products.

(a) Cayenne Pepper Was Not Reviewed By The Advisory Panel As An Active Ingredient Of OTC Nailbiting Or Thumbsucking Products

According to FDA's OTC Drug Review Ingredient Status Report, cayenne pepper has been reviewed under the OTC Drug Review by the Topical Analgesic OTC Advisory Review Panel as a counterirritant for external analgesic use[9/] and by the Dental OTC Advisory Review Panel as a counterirritant and toothache relief ingredient for relief of oral discomfort.[10/] However, cayenne pepper was never reviewed by the Advisory Review Panel on OTC Miscellaneous External Drug Products as an active ingredient in nailbiting and thumbsucking deterrent drug products. In fact, the only ingredients listed in FDA's request for data and reviewed by the Advisory Panel for this indication were denatonium benzoate, isopropyl alcohol, and sucrose octaacetate.[11/] According to the Panel report, the list of active ingredients was compiled on the basis of recognized historical use or use in marketed products as nailbiting and thumbsucking active ingredients. 45 Fed. Reg. 69,122, 69,123 (Oct. 17, 1980). Therefore, the omission of cayenne pepper from this list illustrates that neither the agency nor the Panel considered it to be an active ingredient for purposes of this OTC review.

A review of Docket No. 80N-0146 indicates that FDA never obtained or reviewed any data concerning the use of cayenne pepper as an ingredient in nailbiting and thumbsucking deterrent products.[12/] In an attempt to find some

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9/ See FDA, OTC Drug Review Ingredient Status Report (Dec. 2, 1991); 44 Fed. Reg. 69,768 (Dec. 4, 1979) (capsicum categorized as class I counterirritant).

10/ See FDA, OTC Drug Review Ingredient Status Report (Dec. 2, 1991); 47 Fed. Reg. 22,712 (May 5, 1982) (capsicum categorized as class I for counterirritant; class II for toothache relief ingredient).

11/ See OTC Miscellaneous External and Internal Drug Products Request for Data and Information. 40 Fed. Reg. 38,179, 38,180 (Aug. 27, 1975); Nailbiting and Thumbsucking Deterrent Products, Proposed Rule, 45 Fed. Reg. 69,122, 69,123 (Oct. 17, 1980).

12/ See Table of Contents, Docket No. 80N-0146, entitled, "Nailbiting & Thumbsucking Deterrent Drug Products For OTC Use" (Nov. 23, 1994). Exhibit 10.

reference to cayenne pepper in the administrative record, FDA asserts in a November 1, 1994 letter (see Letter from W. Gilbertson to R. Manthei responding to Oakhurst's 2/20/94 Citizen Petition) that the Advisory Panel's reference to "home remedies such as pepper" indicates that the Panel was aware of the use of cayenne pepper in these OTC products. See 45 Fed. Reg. 69,122, 69,124. This position simply has no basis in fact. We believe the clear and plain meaning of the term "pepper" is "black pepper." Cayenne pepper is a distinct form of pepper obtained from plants of another genus and typically described with a qualifying term, i.e., "cayenne."[13/] There is also evidence from a misbranding case that "pepper" means black pepper in the trade and according to its ordinary usage. See United States v. Seventy-Five Boxes of Alleged Pepper, 198 F. 934, 936 (D.N.J. 1912).

Furthermore, our review of OTC Volume 160020, the volume cited for the proposition that "home remedies such as pepper" were considered by the Panel, revealed no documentation to support this conclusion. However, even if there were evidence that the Panel reviewed home remedies, the Panel's mere reference to pepper does not demonstrate that cayenne pepper was properly considered and

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13/ "Pepper" is defined by Webster's Third New International Dictionary 1674 (1981)as:

> **1a:** a pungent product obtained from the fruit of an East Indian plant (*Piper nigrum*), used as a condiment and sometimes as a carminative or stimulant, and prepared in a form (1) consisting of the entire dried berry or (2) consisting of the dried seeds divested of all membranes and pulp with both forms being usu. ground into powder before use - called also (1) *black pepper*, (2) *white pepper* **b:** any of several somewhat similar products obtained from other plants of the genus *Piper* - often used with a qualifying term; see LONG PEPPER **c:** any of various pungent condiments obtained from plants other than those of the genus *Piper* - used with a qualifying term . . . see CAYENNE PEPPER . . . . **4:** any of numerous plants other than members of the genera *Piper* and *Capsicum* that have pungent or aromatic qualities - usu. used with a qualifying term . . . .

intended to be included within the OTC review. Furthermore, this single statement cannot support the proposition that the Panel was aware of, and reviewed information regarding the use of, cayenne pepper as an ingredient of both nailbiting and thumbsucking deterrent products since the statement only refers to nailbiting.[14/]

Panel reports have consistently provided a carefully prepared scientific analysis of every active ingredient, especially when a determination is made that the ingredient is not effective. The APA requires that an administrative record be prepared on which to base an agency action. The agency cannot come back to and argue that the inclusion of the word "pepper" constitutes a scientific review. Because Miscellaneous External Drug Products record cannot be supported scientifically, FDA should not be permitted to destroy a safe an effective product by administrative fiat.

The administrative record for the TFM shows that FDA incorporated the Panel's review and specifically reviewed only two active ingredients, denatonium benzoate and sucrose octaacetate. 47 Fed. Reg. 39,096, 39,097 (Sept. 3, 1982). In fact, FDA stated that "[i]f neither of these ingredients is elevated to Category I status, there will be no active ingredients to include in a final monograph, and these products will have to be removed from the market." Id. at 39,098. Therefore, it is clear from this statement that FDA did not separately review cayenne pepper or even consider other active ingredients. It is disingenuous for FDA to argue that the fact that the agency proposed Category I labeling in the TFM when no ingredient appeared to be safe and effective "suggests that ingredients other than denatonium benzoate and sucrose octaacetate (e.g., cayenne pepper) . . . are also covered by the TFM."[15/] According to FDA's OTC review procedures, FDA is required to publish a TFM "containing a monograph establishing conditions under which a category of OTC drugs is generally recognized as safe and effective and not misbranded." 21 C.F.R. § 330.10(a)(7)(i).

14/ "Home remedies such as pepper are used in a similar fashion to deter nailbiting." 45 Fed. Reg. 69,122, 69,124 (Oct. 17, 1980).

15/ See November 1, 1994 letter at 3.

Because FDA never obtained any data, and no data was ever submitted, concerning the safety and effectiveness of cayenne pepper as an ingredient for use in nailbiting and thumbsucking deterrents, reference to the ingredient in the final rule as a drug is inappropriate. While FDA suggests that Oakhurst was partially responsible for the limited record, the burden of producing an administrative record to support its determination is on FDA. 21 C.F.R. § 330.10(a)(10)(ii); see also Burlington Trucklines v. United States, 371 U.S. 156, 168 (1962); Rutherford v. United States, 542 F.2d 1137 (10th Cir. 1976), rev'd on other grounds, 442 U.S. 544 (1979). The fact that Oakhurst's predecessor company had the opportunity to submit information regarding cayenne pepper's safety and effectiveness is inapposite because it is possible that the company did not perceive its product to be adversely affected by the OTC monograph process since it believed THUM® to be exempt from the OTC review as a cosmetic and/or an old drug. Regardless of the reason, FDA may not, with no administrative record, list in the final rule for nailbiting and thumbsucking deterrent products an ingredient that is in reality safe and effective. Therefore, Oakhurst requests that the "negative" final rule be revoked and a final monograph be established that lists cayenne pepper and denatonium benzoate as safe and effective ingredients for OTC nailbiting and thumbsucking deterrent drug products.

(b) FDA Violated The APA's Requirements Of Notice And Comment Rulemaking And Its Own Administrative Procedures By Including Cayenne Pepper In The Final Rule For Nailbiting And Thumbsucking Deterrent Products

Because the administrative record does not support the contention that cayenne pepper was reviewed as an active ingredient for nailbiting and thumbsucking deterrent products, it cannot be bootstrapped into the final rule without violating the APA's requirements of notice and comment rulemaking and FDA's own OTC review procedures.

According to the APA, and its interpreting case law, an agency must promulgate rules in accordance with notice and comment procedures specified by section 553 of the APA when it uses rules to set forth substantive policies that will bind the public and impose mandatory obligations. See Chrysler Corp. v. Brown, 441 U.S. 281 (1979); Perales v. Sullivan, 948 F.2d 1348 (2d Cir. 1991); Bellarno Intern. Ltd. v. FDA, 678 F. Supp. 410 (E.D.N.Y. 1988). FDA's final rule on nailbiting and thumbsucking deterrent products is clearly a substantive rule: it prohibits manufacturers from marketing nailbiting and thumbsucking deterrent products containing active ingredients that have not been approved as new drugs

under section 505 of the Act. However, FDA provided no notice or opportunity to comment before adding cayenne pepper to this final regulation. This action was arbitrary and capricious and without observance of procedure required by law.

Furthermore, FDA violated its own OTC review procedures by listing cayenne pepper in the final regulation. An agency is bound to follow the procedures required by its own regulations, even if these regulations were not statutorily or constitutionally mandated. United States v. Nixon, 418 U.S. 683, 695-96 (1974). "It is axiomatic that 'an agency is legally bound to respect its own regulations and commits procedural error if it fails to abide them.'" Algonquin Gas Transmission Co. v. FERC, 948 F.2d 1305, 1315 (D.C. Cir. 1991) (quoting Esch v. Yeutter, 876 F.2d 976, 991 (D.C. Cir. 1989)).

According to FDA's OTC review procedures, the Advisory Panel report shall contain "a statement of all active ingredients, labeling claims or other statements, or other conditions reviewed and excluded from the monograph" and placed under Category II or III. 21 C.F.R. § 330.10(a)(5)(iii). Because the administrative record does not show that the Advisory Panel reviewed cayenne pepper, it is not surprising that the Advisory Panel's report for nailbiting and thumbsucking deterrent products does not include a statement regarding the inclusion or exclusion of cayenne pepper from the monograph.

FDA's OTC review regulations also specifically state that FDA "shall make all decisions and issue all orders pursuant to this section solely on the basis of the administrative record, and shall not consider data or information not included as part of the administrative record." 21 C.F.R. § 330.10(a)(10)(ii); see also 39 Fed. Reg. 19,878 (June 4, 1974) ("[t]he Commissioner is obligated to base his decision with respect to a monograph on the entire administrative record."). Because there is no administrative record to support FDA's addition of cayenne pepper in the final regulation for nailbiting and thumbsucking deterrent products, reference to the ingredient as an example of an ingredient for which there is a "lack of adequate data to establish general safety and effectiveness" is inappropriate and in violation of section 330.10(a)(10)(ii).

Finally, FDA's procedural shift from a positive proposed rule and TFM (affirmatively listing appropriate labeling and conditions of use) to a negative final monograph (listing ingredients and conditions excluded), with no notice or opportunity for comment, was inappropriate and inconsistent with FDA's administrative procedure. FDA's OTC review procedures require negative final monographs to be promulgated in accordance with notice and comment procedures.

21 C.F.R. § 330.10(a)(7)(ii). In fact, FDA stated in its preamble to a final rule revising the OTC review procedures, that "[e]ven if no changes are made [to a panel's recommendations], the public should have notice of the agency's position on the matter and have an opportunity to respond to it before a final rule is adopted." 46 Fed. Reg. 47,730 (Sept. 29, 1981).

While FDA issued a tentative and final rule establishing the active ingredients excluded from the OTC monograph for nailbiting and thumbsucking, see 55 Fed. Reg. 20,434 (May 16, 1990) and 55 Fed. Reg. 46,914 (Nov. 7, 1990) (reserved at 21 C.F.R. § 310.545(a)(13)), neither of these rules list cayenne pepper. Therefore, the sudden inclusion of cayenne pepper in the final rule on nailbiting and thumbsucking deterrent products and its implicit inclusion in section 310.545,[16/] is improper, in violation of FDA's administrative procedure, and an unjust denial of petitioner's administrative rights. See Bowman Transp., Inc. v. Arkansas Best Freight Syst. Inc., 419 U.S. 281, 285 (1974) ("[t]he agency must articulate a 'rational connection between the facts found and the choice made'") (citation omitted); Rutherford v. United States, 616 F.2d 455, 456 (10th Cir.), cert. denied, 499 U.S. 937 (1980) (FDA cannot "escape the obligation of producing an administrative record to support its determination . . . . such a conclusory ruling precludes effective review under 5 U.S.C. Section 706(2)." (quoting Rutherford, 542 F.2d at 1143)).

Furthermore, according to section 330.10(a)(7)(ii), active ingredients can be excluded from a monograph only upon the FDA's "determination that they would result in a drug product not being generally recognized as safe and effective or would result in misbranding . . . ." Id. Because cayenne pepper has never been reviewed by the panel or the FDA as an active ingredient in nailbiting and thumbsucking deterrent products, there has been no finding by FDA, other than its conclusory assertions in the final rule and the November 1, 1994 letter, that cayenne pepper is not safe and effective or its use would result in such products' misbranding. Therefore, we request that the agency revoke 21 C.F.R. § 310.536 and establish a "positive" monograph for OTC nailbiting and thumbsucking deterrent

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16/ FDA stated in the preamble to the final rule for nailbiting and thumbsucking deterrent products that it is listing all OTC nailbiting and thumbsucking active ingredients in section 310.536, "in order to avoid duplication . . . Accordingly, § 310.545(a)(13) is being removed." 58 Fed. Reg. 46,749, 46,753-54 (Sept. 2, 1993).

drug products which lists cayenne pepper and denatonium benzoate as "monographed" ingredients.

3. The THUM® Product, Containing Cayenne Pepper, Is An Old Drug, Which Is Legislatively Outside The Administrative OTC Review

In the alternative, Oakhurst requests that FDA amend 21 C.F.R. § 310.536 to remove all references to cayenne pepper and provide the firm with an official agency recognition of THUM®'s old drug status.

The 1938 amendments to the Act imposed for the first time a preclearance requirement for drugs for which safety was not generally recognized. Drugs not on the market as of the date of passage of the 1938 amendments to the Act for which safety was a question were "new drugs" and had to obtain a New Drug Application ("NDA"). Drugs on the market after June 30, 1906, and prior to the enactment of the 1938 amendments to the Act, fell within a "grandfather clause" exemption to the new drug provisions of the Act. Congress provided this legislative exemption for "old drugs," because it recognized that products in the marketplace before the passage of the statute were safe and should not retroactively become the subject of NDAs. These drugs were allowed to remain on the market as old drugs, provided the labeling for the drugs contained the same representations concerning conditions for their use as their pre-1938 labeling.[17/]

FDA, in 1972, by regulation, created the OTC Review, which is a quasi-scientific administrative process to determine which active ingredients are recognized as safe and effective for use in OTC products. In the administrative process, the agency proposed to make a determination of ingredients that were safe and effective; those failing to meet that standard would require new drug applications. To the extent that a product contains an active ingredient that had not been marketed prior to 1962 and effectiveness was not established, the application of this procedure is correct; to the extent that an ingredient was not safe and was marketed after 1938, the application of this procedure is also correct.

17/ See FFDCA, § 201(p)(1), 21 U.S.C. § 321(p); United States v. Allan Drug Corp., 357 F.2d 713 (10th Cir. 1966), cert. denied, 385 U.S. 899 (1966).

However, for any product marketed prior to 1938, the mere marketing provides a legislative exemption as long as the labeling contains the same representations. To conclude otherwise is to suggest that Congress intended to accomplish absolutely nothing with the grandfather provision.

Even though THUM® has been marketed since 1935, the agency has advanced two arguments as to why THUM® is not entitled to the protection of the grandfather clause in its November 1, 1994 letter. The first is that all drugs, even old drugs, are subject to the OTC Review's misbranding provisions. This argument improperly expands the reach of the misbranding provisions of the Review to render the legislative exemption meaningless. Under this reading, drugs that were specifically exempted from the safety and effectiveness criteria of the new drug provisions are now subject to a safety and effectiveness criterion under the misbranding provisions of the OTC Review regulations. Indeed, the FDA explicitly acknowledged this effect in its proposed and final rule establishing the procedures for the classification of OTC drugs. See 37 Fed. Reg. 85, 86 (Jan. 5, 1972); 37 Fed. Reg. 9464, 9472 (May 11, 1972). This construction of the misbranding provisions offends the well-settled rule of statutory construction that all parts of a statute, if at all possible, are to be given effect. Weinberger v. Hynson, Westcott & Dunning, Inc., 412 U.S. 609, 633 (1973); Jarecki v. G.D. Searle & Co., 367 U.S. 303, 307 (1961). FDA cannot, by administrative fiat, issue rules that contravene the clear meaning of the statutory grandfather clause. In so doing, FDA would be negating a legislative provision clearly calculated to protect companies marketing old drugs.

Furthermore, even if the misbranding provisions of the Review could properly be applied to old drugs, there is no documentation to support FDA's conclusion that nailbiting and thumbsucking deterrent products containing cayenne pepper are misbranded. According to Allan Drug, the burden is on the government to prove in court that a drug's labeling claims do not have their claimed effect when the drug is already on the market and has never been subject to the new drug procedures. 357 F.2d at 718.

Administratively, the FDA has never made such a finding. As discussed in Section II.A.2., the administrative record does not include any scientific review of cayenne pepper. FDA's advisory panel did not review cayenne pepper and there is no discussion concerning cayenne pepper in either the Panel report or TFM. FDA is simply engaging in circular reasoning by referring to section 310.536(b) as support for the proposition that THUM® is misbranded. Since there is no evidence from the administrative record to support a finding that nailbiting and thumbsucking deterrent products containing cayenne pepper are not effective, FDA's conclusory

reference to this section is insufficient to find that THUM® is misbranded. See Rutherford v. United States, 616 F.2d at 456 (FDA cannot "escape the obligation of producing an administrative record to support its determination . . . that [a product] is a new drug, for it is not a new drug merely because they say it is.") (quoting Rutherford, 542 F.2d at 1143). In fact, as discussed in Section II.A.1, scientific expert opinions and clinical evidence exists that aversive taste therapy products such as THUM® are safe and effective.

The second argument advanced by FDA is that the product is not entitled to, or has lost the exemption to, the new drug provisions of the Act because of changes made to the product's labeling and formulation. We disagree.

According to the 1938 grandfather clause, a product will not be recognized as a "new drug" "if at any time prior to the enactment of this Act it was subject to the Food and Drugs Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use." FFDCA § 301(p), 21 U.S.C. § 321(p). Therefore, to be entitled to the exemption under the 1938 grandfather clause, a product must have been marketed before June 25, 1938 and the current labeling must indicate the same conditions of use and composition as the pre-1938 product.

While courts have held that this exemption should be construed strictly against the party that invokes it, United States v. Allan Drug Corp., 357 F.2d at 718, the government must prove by a preponderance of evidence that a product is a new drug. United States v. An Article of Drug . . . Bentex Ulcerine, 469 F.2d 875, 878 (5th Cir. 1972), cert. denied, 412 U.S. 938 (1973). Minor changes that do not affect the products conditions for use or minor changes in the product's formulation should not necessarily result in a product's loss of the exemption. See Allan Drug, 357 F.2d at 719; see also United States v. Articles of Drug . . . Alcon Laboratories, Inc., 745 F.2d 105, 111 (1st Cir. 1984), cert. denied, 470 U.S. 1004 (1985); United States v. 50 Boxes . . . Cafergot P-B, 721 F. Supp. 1462, 1468 (D. Mass. 1989), aff'd, 909 F.2d 24 (1st Cir. 1990). Because THUM® has been continuously marketed since 1935 and its conditions of use and composition have not changed since the product was first introduced in 1935, THUM® meets the old drug criteria under the 1938 grandfather clause.

THUM® has been marketed as a nailbiting and thumbsucking deterrent product continuously since 1935. Exhibit 1 contains a copy of a United States Patent Office Statement indicating that the trademark THUM® was registered with the U.S. Patent Office on November 5, 1935, as a preparation for the

prevention of nailbiting and thumbsucking. The Registration Statement also indicates that the trademark had been "continuously used and applied to said goods in applicant's business since January 1, 1935." Also included in Exhibit 1 is a Certificate of Renewal from The United States Patent Office, dated January 31, 1956, indicating that the original trademark was registered on November 5, 1935.

Oakhurst is the successor manufacturer of THUM® and has not been privy to all prior information and efforts with respect to the marketing of THUM®. To date, Oakhurst has clearly demonstrated that THUM® was marketed in 1935 and that the product was always intended to be used as a nailbiting and thumbsucking deterrent product. What Oakhurst has not been able to identify is a copy of the label that appeared on the product prior to 1938. The earliest examples of the labeling for the THUM® product that Oakhurst has been able to locate are from the 1948-49 Drug Topics Red Book and the 1952 American Druggist Bluebook. See Exhibits 11 and 12. Both the 1948 and 1952 labeling represent the product as an aid to discourage thumbsucking and nailbiting. Therefore, these examples demonstrate that the indications for use of the product have remained unchanged.[18/]

FDA also asserts that a comparison of the 1948 labeling and the current label shows that the product labeling has changed. This position has no merit. The current product label states, "ACTIVE INGREDIENTS: Cayenne pepper extract,

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18/ While the court in United States v. Articles of Drug for Veterinary Use . . . Goshen, No. 80 Civ. 3486-CSH, 1981-1982 FDLI Jud. Rec. 102 (S.D.N.Y. May 28, 1982), found claimant's assertions that the relevant veterinary products were in use before 1938 and copies of invoices dated from 1945 to be irrelevant with respect to the 1938 grandfather clause because no proof that the product was manufactured before 1938 was submitted, this case can be distinguished because Oakhurst has submitted evidence that the product was manufactured before 1938 (i.e., the trademark certificates). Oakhurst also has copies of the labeling in use in 1948 and signed affidavits attesting to the pre-1938 use of the product. See Exhibits 11, 14 through 17. Additionally, Oakhurst has submitted affidavits attesting that the product's formulation has not changed since 1935. Exhibits 14 through 17. In contrast, the claimant in Goshen admitted to having altered the formulation of one of the relevant products.

citric acid. Also contains isopropyl alcohol, acetone, lacquer." Exhibit 13. The 1948-1949 Drug Topics Red Book states that "THUM contains extract of capsicum (2.34%) in a base of acetone nail lacquer and isopropyl alcohol." See Exhibit 11. While "citric acid" is specifically listed in the current label and not in the 1948 labeling, it is clear from the original formula for THUM® that citric acid was always an integral component of the product. See Exhibit 18 (Exhibits 14-17 certify to the authenticity of the formula and the fact that the same formula is currently in use).[19/] Therefore, this is not a significant change to the product labeling. The only other difference between the two product descriptions is the current use of the word "cayenne pepper" instead of "capsicum." However, these two words are formally recognized alternate names for each other.[20/]

Similarly, FDA's allegation that there is no evidence that the concentration of capsicum has remained the same since 1948, has no merit. The affidavits attached to this Petition attest to the continued use of Dr. Frawley's original formulation for

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19/ Exhibit 18 contains a copy of the original formula for THUM® in the handwriting of R.D. Frawley, D.D.S., the founder of Num Specialty Company and the inventor of THUM®. Exhibit 14 is a certification from Mr. Benjamin M. Deavenport, Vice President of Numark, Inc., the company that purchased THUM® from Num Specialty Company in 1981. Mr. Deavenport certifies that at the time of purchase of THUM®, the formula which appears in Exhibit 18 was in Dr. Frawley's handwriting and represented the original formula for THUM® as marketed by Dr. Frawley since 1935. Exhibit 15 contains an affidavit from Mr. George Allen, a nephew of Dr. Frawley's and a former Vice President of Num Specialty Company. Mr. Allen verifies that the formula appearing in Exhibit 18 is the original formula. Exhibit 16 contains a certificate from Ms. Lisa Sherman, grand niece of Dr. Frawley. Ms. Sherman certifies that the master formula with the initials "I.B.F." is a true and accurate copy of the formula for THUM® that was sold to Mr. Deavenport and Numark, Inc. Exhibit 17 contains an affidavit from Mr. Stanley H. Roberts, the President of Oakhurst. In his affidavit, Mr. Roberts states that the formula currently used to manufacture THUM® is the same formula that Oakhurst received from Numark, Inc.

20/ See The Pharmacopeia of the United States of America 105 (indicating that an alternate name for cayenne pepper is capsicum).

THUM® and thereby demonstrate that the concentration has not changed. See Exhibits 14-17. FDA clearly would not have asserted that the petitioner provided no evidence of "past and present quantitative formulas" showing that THUM®'s formula has always been the same if it had reviewed the above mentioned exhibits. FDA's Nov. 1, 1994 letter at 4. These exhibits include a copy of the original formula and formulation for the production of THUM® and certifications by the current and prior owners of THUM® that the identical formula has been in use since the inception of the product. Therefore, petitioner submits that it has demonstrated that the formula for THUM® has remained the same from its introduction in 1935 to date.

The Supreme Court has held that the grandfather clause exempts drugs "so long as their composition and labeling remained unchanged." USV Pharmaceutical Corp. v. Weinberger, 412 U.S. 655, 663 (1973). Petitioner believes the above changes, when both taken by themselves and compared to the changes at issue in past grandfather clause cases, are so insignificant that they do not prevent THUM® from maintaining its old drug status. A review of the case law addressing both the 1938 and 1962 grandfather clauses supports this conclusion. For example, in Alcon Labs the court found that the conditions for use of a rectal suppository ("WANS") had "changed significantly" due to the following changes: the pre-1962 labeling lists 11 specific causes for nausea and vomiting under "indications" and states that children of all ages tolerate WANS well. The current labeling does not indicate causes therefore implying that it treats conditions not listed in the pre-1962 labeling. It also states under "indications" that the product should not be used in infants below the age of 6 months and is not recommended for treatment of uncomplicated vomiting in children. 745 F.2d at 115. The court concluded that it does not "view this labeling change as simply a minor correction . . . . [i]nstead it indicates that new information . . . has become available . . . . This new information and WANS's changed labeling, indicate that the 'existing claims' made for WANS . . . are no longer accurate." Id.

In Cafergot P-B, the court similarly found significant changes between the pre-1962 CPB Suppository label and the label in current use. 721 F. Supp. at 1468. For example, the pre-1962 label recommends that it be used to treat an existing headache. It also recommends use for children and the use of up to four suppositories a week. The current label recommends use to prevent a headache, includes a warning that its use in children is contraindicated and expands the number that can be used in a week to five. Id. at 1468-69. In many cases, the effect of the change in labeling was to reduce the use of the drug under conditions prescribed or recommended in the labeling or expand the warnings applicable to the

product. See, e.g., Allan Drug, 357 F.2d 713; SmithKline Corp. v. FDA, 587 F.2d 1107 (D.D.C. 1978). In other cases, companies either fail to allege that all product ingredients are the same, including both active and inactive ingredients, or an ingredient was removed or added to the formulation. See, e.g., United States v. Undetermined Quantities of an Article . . . (Anucort), 709 F. Supp. 511 (D.N.J. 1987), aff'd mem., 857 F.2d 1466 (3d Cir. 1988); Rutherford v. United States, 616 F.2d 455. None of these fact patterns are similar to those in THUM®. The change in labeling from "capsicum" to "cayenne pepper" does not reduce or expand the use of the product; the addition of citric acid to the current label does not reflect the addition of a new ingredient to the product; and the attached statements from prior owners of THUM® attest to the continued use of the original formulation from 1935 forward.

Because the policy behind the Act is to protect the public from dangerous drugs, petitioner urges FDA to agree that THUM® meets the criteria for the 1938 grandfather clause exemption. If the FDA concludes that the above minor modifications are sufficient for the product to lose its exemption to the new drug provisions, then the congressional grandfather clause will have no meaning. FDA would be sending the message that no product will be considered an old drug. This would have the result of administratively eviscerating a congressionally mandated exemption to the new drug provisions. The legislation in 1937 foresaw the exact effort that is occurring some 63 years later. FDA is seeking to remove a safe and effective product from the market -- not based on new data or scientific evidence, but on an administrative process. Clearly THUM® is the subject of expert opinion and studies and yet FDA, relying on an administrative process that is devoid of an administrative record, is seeking to remove a safe and effective product. Congress specifically forbade the very act that FDA is currently engaged in perpetrating.

Should FDA find that the 1935 trademark certificate and the affidavits of the relatives of the original owner of THUM® are insufficient evidence of pre-1938 use for THUM® to qualify for old drug status under the 1938 grandfather clause, petitioner posits that THUM® clearly fits within the old drug definition of the 1962 Drug Amendments.[21/] With the 1962 Drug Amendments, Congress added the requirement of a general consensus among qualified experts as to the efficacy of a

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21/ See Pub. L. No. 87-781, § 107(c)(4), 76 Stat. 780, 789.

drug. The 1962 grandfather clause exempted drugs from the new drug provisions of the Act "when intended solely for use under conditions prescribed, recommended, or suggested in labeling" as of October 9, 1962. To qualify for the 1962 grandfather clause exemption, the drug must meet the following three conditions: (1) the drug must have been commercially used or sold prior to October 10, 1962 for the same uses for which it is presently being sold; (2) there must be no effective NDA for the drug on October 10, 1962; and (3) the drug must not be a "new drug" as defined by the 1938 Act, i.e., there must be general consensus among qualified experts as to the safety of the drug. See Alcon Labs., 745 F.2d at 108; Tyler Pharmacal Distributors, Inc. v. United States, 408 F.2d 95, 99 (7th Cir. 1969).

THUM® clearly meets these conditions. As demonstrated above, (1) THUM® has been in commercial distribution since 1935 and has been manufactured using the same formula and marketed for the same uses for which it is presently being sold. See 1935 Trademark certificate (Exhibit 1), 1948, 1952 and current labeling (Exhibits 11 - 13), and the attached affidavits (Exhibits 14 - 17); (2) THUM® was never the subject of an NDA; and (3) THUM® does not meet the 1938 Act's definition of a "new drug."

The 1938 Act defined "new drug" as "[a]ny drug the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety of drugs, as safe for use under the conditions prescribed, recommended, or suggested in the labeling thereof . . . ."[22/] THUM® does not meet this definition because it was generally recognized as safe prior to 1962 as shown by the attached report summarizing two studies which evaluated the use of THUM® for discouraging nailbiting and thumbsucking in 1940 and 1949. See Exhibit 19. This study demonstrates that scientific testing for safety was performed prior to 1962 and that THUM® was, and is, non-toxic. See Alcon Labs., 745 F.2d at 115; Cafergot P-B, 721 F. Supp. at 1469; Durovic v. Richardson, 479 F.2d 242, 251 (7th Cir. 1973), cert. denied, 414 U.S. 944 (1973).

Furthermore, THUM®'s main ingredient, cayenne pepper, is listed as a substance that is "generally recognized as safe" in food based on common use prior to January 1, 1958. See 21 C.F.R. § 182.10; FFDCA § 201(s), 21 U.S.C. § 321(s).

22/ Act of June 25, 1938, ch. 675, § 201(p), 52 Stat. 1040.

Because the standard for food safety is generally higher than that for any other regulated product, it is clear that THUM® does not have a safety problem. This conclusion is further supported by more recent documentation in scientific journals and the popular press, including the attached certifications by Drs. Friman and Schmitt, attesting to the safety of THUM®.

Therefore, THUM® is an old drug that is subject to the statutory exemption from the new drug provisions of the Act under the grandfather clause exemptions contained in the 1938 and 1962 Acts. As a result, cayenne pepper, when used as a nailbiting and thumbsucking deterrent, does not fall within the review of the OTC Drug Review procedure. Accordingly, Petitioner requests that 21 C.F.R. § 310.536 be revoked and that the FDA officially recognize the old drug status of the THUM® product..

B. Denatonium Benzoate

Denatonium benzoate (0.35 % or less) was reviewed by the Advisory Review Panel on OTC Miscellaneous External Drug Products and determined to be a safe thumbsucking and nailbiting deterrent when topically applied on children 4 years of age and over. 45 Fed. Reg. at 69125. The Panel, however, recommended that denatonium benzoate be placed in "Category III" because it was unaware of the existence of sufficient data to determine the ingredient's effectiveness as a thumbsucking and nailbiting deterrent. See id. The FDA subsequently concurred with the Panel's recommendation. See 47 Fed. Reg. at 39097.

Numerous controlled studies conducted since the Panel's review unequivocally demonstrate that denatonium benzoate is a safe and effective ingredient for nailbiting and thumbsucking deterrence. Therefore, Oakhurst requests, that FDA revoke 21 C.F.R. § 310.536 and concurrently issue a regulation under the section reserved for nailbiting and thumbsucking deterrent products, 21 C.F.R. pt. 358, subpt. C, declaring that an OTC nailbiting and thumbsucking deterrent product in a form suitable for topical administration is generally recognized as safe and effective and is not misbranded if it contains denatonium benzoate at levels of 0.35% or less. A proposed regulation is enclosed as Appendix A.

As discussed in section II.A.1.b, above, Dr. Patrick C. Friman has conducted and published five separate studies that demonstrate the effectiveness of denatonium benzoate as a thumbsucking deterrent ingredient. See Exhibit 3. All of these studies were conducted with the "Stopzit" brand aversive taste therapy

product, which contains denatonium benzoate. Additionally, Dr. Friman has recently conducted another controlled study that confirms that aversive taste therapy products in general, and those containing denatonium benzoate specifically, are an effective treatment for the thumbsucking habit in children. See Exhibit 2, Attachment B. This latest study is expected to be published in a forthcoming issue of Pediatrics. As noted above, the effects of Dr. Friman's studies can be extrapolated to nailbiting behavior. See supra n. 3.

The combined effect of the studies referenced in this petition and the generally recognized effectiveness of aversive taste therapy products in general (see above), provides an overwhelming body of scientific evidence supporting the safety and effectiveness of denatonium benzoate as a thumbsucking and nailbiting deterrent ingredient. Accordingly, Oakhurst requests that FDA issue a regulation under 21 C.F.R. pt. 358 declaring denatonium benzoate to be a "monographed" ingredient for OTC nailbiting and thumbsucking deterrent drug products.

C. Nailbiting And Thumbsucking Deterrents Are Cosmetic Products That Are Outside The Scope Of The OTC Review

In the alternative, Oakhurst requests that FDA recognize that nailbiting and thumbsucking deterrent products containing safe ingredients, such as cayenne pepper and denatonium benzoate, are cosmetics that are outside the scope of the OTC review.

Specifically, Oakhurst disagrees with FDA's contention that all nailbiting and thumbsucking deterrents are drugs within the meaning of section 201(g) of the Act (21 U.S.C. § 321(g)). See November 1, 1994 letter. Oakhurst respectfully submits that thumbsucking/nailbiting deterrents are very clearly not drugs, but rather are cosmetics for the following reasons: (1) Nailbiting and thumbsucking are habits and not diseases, therefore products that deter such habits should not be regulated as drugs; (2) THUM®, and other thumbsucking / nailbiting deterrent products, are intended to be used as cosmetics; and (3) The OTC review is not meant to determine whether a product is making cosmetic claims.

(1) Nailbiting And Thumbsucking Are Habits And Not Diseases, Therefore Products That Deter Such Habits Should Not Be Regulated As Drugs

The FDA acknowledges that nailbiting and thumbsucking are "habits" which, if left untreated, could lead to medical problems. 58 Fed. Reg. 46,749, 46,750 (Sept. 3, 1993). The Advisory Panel in the original proposed rule noted that "fingernail

biting is an extremely common habit." 45 Fed. Reg. 69,122, 69,123 (Oct. 17, 1980). The same panel concluded that thumbsucking was a "natural act in the newborn" and "an empty or simple habit, as a result of learned behavior." Id. at 69,124.

Thumbsucking is defined in the dictionary as: "[T]he habit of sucking a thumb beyond the period of physiologic need." Webster's New Third International Dictionary 2387 (1981) (emphasis added). Nailbiting is defined as a "habitual biting at the fingernails usu. being symptomatic of emotional tensions and frustrations" or "an act or instance of this behavior." Id. at 1500 (emphasis added). Neither habit is listed or classified in any recognized medical texts as diseases. See, e.g., Stedman's Medical Dictionary (5th ed. 1982) and Dorland's Medical Dictionary (27th ed. 1994).

The legislative history of the Act does not define or discuss the definition of "disease" for purposes of the Act. Thus, under fundamental principles of statutory construction, the commonly used definition is to be used. Perrin v. United States, 444 U.S. 37, 42 (1979); Burns v. Alcala, 420 U.S. 575, 580-81 (1975). The plain meaning of "disease"[23/] does not include a "habit."[24/]

23/ Dorland's Illustrated Medical Dictionary (28th ed. 1994) defines a "disease" as:

> any deviation from or interruption of the normal structure or function of any part, organ, or system (or combination thereof) of the body that is manifested by a characteristic set of symptoms and signs and whose etiology, pathology, and prognosis may be known or unknown.

Id. at 478.

Webster's New Third International Dictionary defines a "disease" as:

> 1 a obs: lack of ease: DISCOMFORT, UNEASINESS, TROUBLE, DISTRESS b (1): an impairment of the normal state of the living animal or plant body or of any of its components that interrupts or modifies the performance of the vital functions, being a response to environmental factors (as malnutrition, industrial hazards, or climate), to specific infective agents (as

(Footnote cont'd on next page.)

The definition of a drug[25/] would have to be stretched beyond all reasonable limits for it to include any behavioral pattern or habit that if left modified, could

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> worms, bacteria, or viruses), to inherent defects of the organism (as various genetic anomalies), or to combinations of these factors: SICKNESS, ILLNESS (2): a particular instance or kind of such impairment (baby-pig) (hampered by her): MALADY, AILMENT - compare HEALTH c: disorder or derangement (as of the mind, moral character, public institutions, or the state) d: an alteration that impairs the quality of a product usu. caused by the action of microorganisms (the . . .'s of wine) 2a obs: a cause of discomfort or harm b: an organism that causes disease - used chiefly in plant pathology.

Id. at 648.

24/ "Habit" is defined in Webster's Third New International Dictionary, as:

> 1 archaic a: CLOTHING, APPAREL . . . 4a: bodily appearance or makeup . . .7a: a behavior pattern acquired by frequent repetition or developed as a physiologic function and showing itself in regularity . . . or increased facility of performance or in a decreased power of resistance . . . b: an acquired or developed mode of behavior or function that has become nearly or completely involuntary . . . .

Id. at 1017.

25/ For purposes of regulation under the Act, a "drug" is defined as:

(Footnote cont'd on next page.)

possibly lead to an injury or disease. Using FDA's reasoning, any cosmetic would be considered a drug where a habit of non-use may develop and a disease or injury could result from such non-use. Examples of products that might be affected include: (1) flavored toothpastes or mouthwashes; (2) shampoos; (3) body lotions; (4) baby lotions; and (5) other products used for personal cleanliness. The non-use of these products could clearly result in a disease or injury, for example, dental cavities, scalp disease, skin irritation or diaper rash.

In a similar vein, it would be farcical for the agency to declare manicures[26/] to be drugs and mittens and gloves[27/] to be medical devices because they could be used to reduce the nailbiting and thumbsucking habits. Furthermore, using the agency's logic, any product that is used to prevent a habit that could result in the development of a disease or injury would be considered a drug. The application of this position leads to the following illogical conclusions: (1) nail polish products applied to fingers to beautify nails are drugs because they could prevent nail breakage which could lead to infection; (2) chewing gums and hard candies are drugs because the could be used to distract smokers from their desire to smoke

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> (A) articles recognized in the official United States Pharmacopoeia, official Homeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any article specified in clause (A), (B), or (C).

FFDCA § 201(g), 21 U.S.C. § 321(g).

26/ Leung, K.C. and Robson, L.M. "Nailbiting," Clin. Pediatrics, 29:690, 692 (1990) (see Exhibit 5).

27/ Id.; see also Friman, P.C. and Schmitt, B.D., "Thumbsucking: Pediatricians' Guidelines," Clin. Pediatrics, 10:438, 440 (1989) (see Exhibit 5).

which could reduce the risk of cancer; and (3) lipstick products used to beautify the lips are drugs because they could discourage the biting of ones lips which could cause infection.

Additionally, petitioner believes the FDA has over-simplified the concept of a "habit." A comprehensive review of the medical literature on the subject shows that current medical thinking places nailbiting and thumbsucking in the category of "habits" and not physiological diseases. See certifications of Drs. Friman (Exhibit 2, Attachment C ¶ 5) and Schmitt (Exhibit 6, ¶ 5). While some thumbsucking and nailbiting habits are extremely severe and may cause, or be a manifestation of, clinically significant conditions, thumbsucking and nailbiting are often "empty habits" that present little medical risk and are often discontinued naturally, or through some kind of reinforcement, during the preschool years.[28/] Additionally, studies have shown that thumbsucking is a universal behavior in infants and is observed in over forty percent of children between three-four years of age. See certifications of Drs. Friman (Exhibit 2, Attachment C ¶ 5) and Schmitt (Exhibit 6, ¶ 5). It is ludicrous to suggest that children younger than four years of age are engaged in normal developmental behavior and at four years and one-day are diseased. Additionally, the published literature suggests that nailbiting and thumbsucking remedies are often sought because such oral habits are perceived as socially unacceptable behaviors.[29/] Therefore, it is more appropriate to say that

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28/ See, e.g., "Thumbsucking: Pediatricians' Guidelines," Clin. Pediatrics, 10:438 (1989) (Exhibit 5); Johnson, E.D. and Larson, B.E. "Thumb-sucking: Classification and Treatment," J. of Dent for Childr., 60:392 (1993) (Exhibit 20); Leung, K.C., and Robson, L.M. "Thumbsucking," Am. Fam. Phys., 44:1724 (1991) (Exhibit 21); "Aversive Taste Treatment of Finger and Thumb Sucking," Pediatrics, 78:174 (1986) (Exhibit 3); Pray, W.S. "Adverse Effects of Finger Sucking and Nailbiting," Pharmacist, 18:43 (Dec. 1993) (Exhibit 22); "Parent & Child," New York Times (Sept. 2, 1993) (Exhibit 7).

29/ See, e.g., 45 Fed. Reg. at 69,124; "Nailbiting," Clin. Pediatrics, 29:690 (Exhibit 5); Friman, P.C. et al. "Influence of Thumbsucking on Peer Social Acceptance in First-Grade Children," Pediatrics, 91:784 (1993) (Exhibit 23); "Little Creatures of Habit," Child (June/July 1991) (Exhibit 7); "Nailbiting, A Handy Guide to Help Kids Deal With the Habit," Joliet (Ill) Herald-News (Mar. 20, 1988) (Exhibit 9).

aversive taste therapy products such as THUM® and Stopzit are primarily intended to discourage empty, "inappropriate" habits rather than to prevent disease.

Both Drs. Friman and Schmitt agree with the above proposition and certify that it is their opinion, based on published medical literature and their own clinical experience, that the nailbiting and thumbsucking habits manifest themselves along a spectrum of severity and risks. While there may be some individuals that require more aggressive treatment and medical intervention because of the severity of the habit, it does not serve the public to remove products that may be successfully used in the less severe cases. "FDA [should] not evaluate the benefit of over-the-counter aversive taste therapy products [such as THUM®] on the basis of their effectiveness in treating the severe habit requiring medical intervention." See Exhibit 2, Attachment C, ¶ 6 and Exhibit 6, ¶ 6. In fact, FDA has not required other OTC products to be effective in all medical circumstances. If it did, OTC products such as aspirin would have to be removed from the market because while aspirin is useful for treating headaches, it cannot effectively treat brain cancer. Petitioner cannot believe that FDA intends this result.

Therefore, petitioner submits that it is clear from the common definitions of the terms, "nailbiting," "thumbsucking," "habit," and "disease," that nailbiting and thumbsucking are not diseases. Since habits manifest themselves along a spectrum of severity with only the most severe requiring medical intervention, products used to deter habits should not be regulated as drugs.

(2) THUM® Is Intended To Be Used As A Cosmetic

A look at the labeling for THUM® reveals that the product's intended use is cosmetic. The labeling says nothing, explicitly or implicitly, about inflammation, infection, digestive problems or any other "disease condition." Rather, the labeling claims that the product "Stops Thumb Sucking and Nail Biting" and "Lets nails grow longer and naturally beautiful." See Exhibit 13. These are not claims that any consumer would be likely to associate with a disease condition. In fact, to the extent that any claim is being made for the beneficial consequences of helping the

user stop biting his or her nails or sucking his or her thumb, it is that the user's nails will become more attractive as a result -- a quintessentially cosmetic claim.[30/]

According to the Act, manufacturers are under a general duty to avoid the use of any cosmetic ingredient that may render the finished product injurious to users under expected conditions of use. See FFDCA § 601, 21 U.S.C. § 361. Oakhurst meets this requirement in that THUM® contains cayenne pepper extract, a substance that is listed in the food regulations as a generally recognized as safe spice, natural seasoning, and flavoring under 21 C.F.R. § 182.10. THUM®'s other ingredients are commonly used in cosmetics: citric acid, isopropyl alcohol, acetone, and lacquer. All of these ingredients are safe and suitable inactive ingredients.

Because THUM®, and other aversive taste therapy products, are primarily intended to affect appearance and not prevent disease, they should be regulated as cosmetics. An article cannot be classified as a drug for purposes of the Act if there has been no showing by the government of therapeutic intent on the part of the vendor. National Nutritional Foods Assn. v. FDA, 504 F.2d 761 (2d Cir. 1974), cert. denied, 420 U.S. 946 (1975); National Nutritional Foods Assn. v. Mathews, 557 F.2d 325 (2d Cir. 1977). The FDA has explicitly agreed with this proposition, stating that "the intended use of a product is the primary determining factor as to whether a product is a drug, a cosmetic, or both." Vaginal Drug Products for Over-the-Counter Human Use; Withdrawal of ANPR, 59 Fed. Reg. 5226, 5227 (Feb. 2, 1994). In accordance with this position, the FDA withdrew the ANPR after determining that cosmetic claims were included in the OTC monograph. Id. at 5231. In the preamble to this withdrawal, FDA stated that claims that are either solely cosmetic or do not relate in a significant way to the safe and effective use of OTC vaginal drug products are "outside the scope of the OTC drug review." Id. at 5232.

Oakhurst believes that thumbsucking and nailbiting deterrent products that primarily claim to beautify nails by the application of a safe, bitter substance such as cayenne pepper, are similarly cosmetic products. THUM®'s labeling clearly

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30/ "The term 'cosmetic' means (1) articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance." FFDCA § 201(i), 21 U.S.C. § 321(i).

indicates that it is intended to beautify nails; the nailbiting and thumbsucking habits are easily recognized; THUM® can be easily applied to fingertips; and, if used as instructed, THUM® is a successful external reminder of the habit, thereby discouraging the behavior. The safe marketing experience of THUM® during the past sixty-five years also attests to the safety and appropriateness of marketing this product as a cosmetic product.

Therefore, Oakhurst respectfully requests that FDA recognize that thumbsucking and nailbiting deterrent products containing safe ingredients, such as cayenne pepper and denatonium benzoate, are cosmetics that fall outside the OTC review process. The administrative record, marketing history and intended use of products such as THUM® and Stopzit require this result.

(3) The OTC Review Is Not Meant To Determine Whether A Product Is Making Cosmetic Claims

Oakhurst specifically contests FDA's statement that "[t]he agency does not consider the prevention of nailbiting and thumbsucking to be a cosmetic claim."[31/] According to the regulations covering the OTC drug review program, the agency and the expert panel are granted authority to review only drug claims, not cosmetic claims. See 21 C.F.R. pt. 330. In fact, the FDA specifically stated in promulgating the OTC review regulations that "[a]ny product for which only cosmetic claims are made and which is therefore not a drug will not be reviewed." 37 Fed. Reg. 9464, 9473 (May 11, 1972).

FDA stated its agreement with this position in its withdrawal of the ANPR for vaginal products. 59 Fed. Reg. at 5227 (cosmetic claims are "outside the scope of the OTC review"); Id. at 5231 ("cosmetic claims are not within the jurisdiction of the OTC drug review"); Id. at 5229 ("the OTC drug review is intended to be an active ingredient review"). Other examples include FDA's statement in the initial OTC miscellaneous external drug products request for data and information, 38 Fed. Reg. 31,697, 31,698 (Nov. 16, 1973) ("[t]his panel is not charged with reviewing the safety or effectiveness of the use of these ingredients in nondrug products such as cosmetics"); FDA's statement in the TFM for astringent drug products, 54 Fed. Reg. 13,490, 13491 (Apr. 3, 1989) ("[a]ny product marketed solely as a cosmetic need not

31/ See FDA's November 1, 1994 letter at 3.

conform to the final monograph"); and FDA's statement in the TFM for skin bleaching drug products, 47 Fed. Reg. 39,108, 39,114 (Sept. 3, 1982) ("the agency has no objection to cosmetic labeling appearing on these products . . . . provided they conform to the cosmetic labeling requirements of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 362))."

Therefore, Oakhurst does not consider FDA's November 1, 1994 letter and the OTC record on nailbiting and thumbsucking deterrent products to be dispositive on the issue of whether thumbsucking / nailbiting deterrent products containing cayenne pepper or denatonium benzoate are cosmetic products.

D. Conclusion

As petitioner has demonstrated, cayenne pepper and denatonium benzoate are safe and effective ingredients for use in nailbiting and thumbsucking aversive taste therapy products. Petitioner has also shown that FDA has failed to review the published literature and scientific data on aversive taste therapies. Furthermore, experts qualified by training and experience recognize that cayenne pepper and denatonium benzoate are effective as nailbiting and thumbsucking deterrents and widely recommend aversive taste therapy products, such as THUM® and Stopzit, as treatments for nailbiting and thumbsucking. Lastly, the safety and effectiveness of aversive taste therapy product in general, and denatonium benzoate in particular, have been established by numerous controlled clinical studies. Accordingly, Oakhurst requests that the Commissioner revoke 21 C.F.R. § 310.536 and create a monograph under the regulation reserved for nailbiting and thumbsucking deterrent products, 21 C.F.R. pt. 358, subpt. C, establishing cayenne pepper and denatonium benzoate as safe and effective ingredients in OTC nailbiting and thumbsucking deterrent drug products.

In the alternative, petitioner requests that the Commissioner revoke the "negative" final rule, 21 C.F.R. § 310.536, and officially recognize the "old drug" status of the THUM® product containing cayenne pepper, or the status of aversive taste therapy products as cosmetics.

III. ENVIRONMENTAL IMPACT

In accordance with 21 C.F.R. § 25.31(a), Oakhurst believes that the actions requested in this Amendment qualify for a categorical exclusion from the requirements of an environmental assessment.

IV. ECONOMIC IMPACT

Oakhurst will provide data concerning the economic impact of this proposal if requested to do so by the Commissioner pursuant to 21 C.F.R. § 10.30(b).

V. CERTIFICATION

The undersigned certifies, that, to the best of his/her knowledge and belief, based upon information furnished to him/her by Oakhurst, this petition includes all information and views on which the petitioner relies, and that it includes representative data and information known to the petitioner that are unfavorable to the Petition.

Sincerely,

Gary D. Yingling

GLY/mhh
Enclosure(s)
cc: Dr. Charles Ganley (FDA, Dir. Div. OTC Drug Products)
James Morrison (CDER Ombudsman) (w/o enclosures)
Oakhurst Company