

Volume III

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Division of Dockets Management (HFA-305)
Food and Drug Administration
Room 1061
5630 Fishers Lane
Rockville, Maryland 20852

Re: Docket No. 2005D-0240
Draft Guidance for Industry
“Gingivitis: Development and Evaluation of Drugs for Treatment or Prevention”
Published in the Federal Register June 28, 2005
Volume 70 Number 123, pp 37102-37103
Comment: Structure/Function Claim in OTC Oral Antiplaque Products

WhiteHill Oral Technologies, Inc., submits these comments in response to the publication by FDA of the Draft Guidance for Industry, “Gingivitis: Development and Evaluation of Drugs for Treatment or Prevention” published in the Federal Register, June 28, 2005, Vol. 70 Number 123, pp. 38102-37103. WhiteHill manufactures products intended for use in the oral cavity, some marketed for cosmetic purposes and others for drug purposes. Representatives of WhiteHill participated extensively during the public hearings conducted by the Plaque Subcommittee.

In response to the proposed Guidance for Industry, which “focuses on plaque-induced gingivitis”, WhiteHill is submitting three separate and independent comments. (1) These comments address only the structure/function claim in OTC oral antiplaque products. (2) Separate comments address the general reduction and prevention of oral health problems claims applicable to OTC oral antiplaque products. (3) Separate

comments also address the cosmetic claims that are applicable to oral antiplaque products.

WhiteHill agrees with the Division of Dermatologic and Dental Products in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration (FDA) that antigingivitis claims are properly classified as drug claims. Because of its focus on gingivitis as a clinically significant endpoint, however, the FDA failed to consider the evidence presented to the Subcommittee with regard to structure/function drug claims justified by reduction of plaque alone, without consideration of any effect on gingivitis. As is demonstrated below, maintenance of good oral hygiene through the simple reduction of dental plaque is also a clinically significant endpoint for consumers. This hygienically significant endpoint is attained through a statistically and clinically significant reduction in dental plaque. These WhiteHill comments therefore focus solely on the structure/function drug benefits of maintaining good oral hygiene.

Considering the draft Guidance for Industry defines the term, gingivitis, as “plaque-induced gingival disease” that “responds well to oral hygiene and antimicrobial products,” it is disappointing and disconcerting to this member of the oral hygiene industry that the draft Guidance does not expand on the role biofilms play in dental plaque; nor, except for a general reference to “oral hygiene,” does the draft Guidance address the critical role *physical removal of biofilms* plays in maintaining oral health. Accordingly, both of these are covered at length by WhiteHill in the three separate and independent comments included herewith.

WhiteHill manufactures a melt-emulsion of polydimethylsiloxane (silicone) in the food-grade surfactant, poloxamer. As demonstrated in scientific studies submitted by WhiteHill to the Subcommittee and in these comments responding to the proposed draft

Guidance for Industry with respect to structure/function and general oral disease prevention claims, the combination of polydimethylsiloxane and poloxamer is effective in achieving a statistically significant and a clinically significant reduction in dental plaque. This combination was determined by the Subcommittee to be Category I for safety (pages 32274-32275). Because this combination is not intended for use to prevent or treat gingivitis, it was placed in Category III for this use.

I. The Requested FDA Action

The proposed draft Guidance for Industry properly recognizes the effectiveness of antimicrobial active ingredients in combination with “oral hygiene” in achieving a significant reduction of the gum disease, gingivitis. It fails, however, to provide similar recognition of the effectiveness of active ingredients to affect the structure or function of the body in order to help maintain good oral hygiene through the reduction of dental plaque with no claim to an antigingivitis endpoint. The FD&C Act specifically recognizes such claims. Section 201(g)(1)(C) defines the term “drug” to include “articles (other than food) intended to affect the structure or any function of the body of man or other animals.”¹

For the reasons set forth below in these comments, WhiteHill requests that FDA recognize, in the tentative Guidance for Industry, the effectiveness of drug products that help maintain good oral hygiene through the statistically and clinically significant reduction of dental plaque with no gingivitis endpoint. Specifically, WhiteHill requests that FDA amend 21 C.F.R. Part 356 in the following four ways.

¹ 21 U.S.C. 321(g)(1)(C).

A. Section 356.3: Definitions

FDA should add a new Section 356.3(r) to define the term “antiplaque drug” as “a drug applied to the oral cavity to help maintain good oral hygiene.”

B. New Section 356.17: Antiplaque Active Ingredients

FDA should add a new Section 356.17 in order to list safe and effective antiplaque ingredients. This section should list, as one of these active ingredients, the combination of polydimethylsiloxane and poloxamer, in a ratio ranging from 1:1 to 1:100, used at a concentration ranging from .01 to 4 percent for liquid and gel emulsions and other oral care products, and an amount ranging from .01 to 0.2 grams per use for chewing gum, mints, breath strips, and chewable candies² provided that the final product must meet the performance test established in new Section 356.94.

C. New Section 356.67: Labeling of Antiplaque Drug Products

The statement of identity should be established as “antiplaque.” The indication should be “helps maintain good oral hygiene.”

D. New Section 356.94: Testing of Antiplaque Drug Products

FDA should specify the following performance test for every product in order to qualify as an effective antiplaque product to help maintain good oral hygiene: A twenty percent reduction in plaque using one of the following two protocols.

1. Protocol for Evaluating Effectiveness of Antiplaque Products for Maintaining Good Oral Hygiene Without Normal Brushing

A double-blind crossover design is utilized to minimize variances due to subjects' normal plaque growth rates. An effective arm size of 20 to 25 is used, with subjects

² The limitation recommended by the Subcommittee that antimicrobial antigingivitis should be expectorated and not ingested (transcript for May 29, 1998, page 110) does not apply to these combination ingredients, which the Subcommittee noted are used in food and ingested OTC drug products (pages 32274-32275).

individually screened for a minimal baseline Plaque Index (PI) of 1.8 (Turesky Modified Quigley-Hein, or similar). Subjects report for baseline examination after having refrained from brushing for 12 hours. After baseline scoring and rubber cup prophylaxis to reduce the PI to zero, subjects are instructed to refrain from brushing or flossing for 48 hours, during which they use the specified test product or placebo at the specified times throughout the day (typically three to six times, depending on the product type). Final PI is scored at 48 hours and the difference is recorded as "reduction in plaque between brushings" for that test period. Allow at least one week "washout" after the first test period, before the crossover period begins. A statistically significant, average PI reduction of at least 20 percent over the placebo is required to satisfy the criterion of helping maintain good oral hygiene.

2. Protocol for Evaluating Effectiveness of Antiplaque Products for Long-Term Maintenance of Good Oral Hygiene with Normal Brushing

A double-blind, crossover design is used to minimize variances due to subjects' normal plaque growth rates. An effective group size of 20 to 25 is used, with subjects individually screened for a minimal baseline PI of 1.8 (Turesky Modified Quigley-Hein, or similar). Subjects report for baseline examination after having refrained from brushing for 12 hours. After baseline scoring and rubber cup prophylaxis to reduce the PI to zero, subjects are instructed to continue their normal brushing habits, but not use any mouth rinses, mints, or gums during the test period. Test periods should be not less than 14 days, preferably 30 days. During the test the subjects use the specified product or placebo at the specified times throughout the day (typically three to six times, depending on the product type). Final PI is scored and the difference is recorded as "reduction in plaque over normal oral hygiene". Allow at least two weeks "washout" after the first test

period, before the crossover period begins. A statistically significant, average PI reduction of at least 20 percent over the placebo is required to satisfy the criterion of helping maintain good oral hygiene.

II. Dental Plaque is a Part of the Structure or Function of the Body of Man

A. The Determinations of the Subcommittee

In its report of May 29, 2003 to FDA, the Subcommittee made a number of extremely important determinations relating to plaque (pages 32236-32239) that directly support WhiteHill's emphasis on the crucial importance of reducing and controlling plaque in order to help maintain good oral hygiene.

The Subcommittee begins by pointing out that "Plaque has a critical etiological role in the development of dental caries, gingivitis, and periodontal disease." These are, of course, the three primary oral health problems that are endemic throughout the United States. Unfortunately, the Subcommittee failed to pursue this scientific determination to the logical conclusion that reduction of dental plaque will help maintain good oral hygiene. The FDA, in their draft Guidance for Industry, is hereby requested to pursue this scientific determination to the logical conclusion that reduction of dental plaque will help maintain good oral hygiene.

As the Subcommittee recognized, there is wide variation in the composition of dental plaque among individuals. Plaque differs both qualitatively and quantitatively in its bacterial content. The Subcommittee stated that:

"This difference in bacterial composition has a major effect on its pathogenic potential both for periodontal diseases and caries. Some dental plaques are not pathogenic or associated with disease, whereas others are etiologic factors for caries and periodontal diseases. However, the two types of plaque cannot be distinguished visually."

Accordingly, the Subcommittee determined that “It may be prudent to treat all plaques as having pathogenic potential.”

WhiteHill agrees completely. All dental plaque is a risk factor for oral health problems. Reduction of dental plaque is therefore of vital importance in helping to maintain good oral hygiene. The FDA is hereby requested, in their draft Guidance for Industry, to treat all plaque as having pathogenic potential.

The Subcommittee went on to state that nonspecific plaque control is essential to the prevention and reduction of oral health problems:

“‘Nonspecific’ plaque control involves decreasing the entire microbial mass in a nonspecific manner, *i.e.*, without any attempt at differentially removing or suppressing any particular bacterial species, although shifts in bacterial composition may occur.”

The Subcommittee specifically noted that nonspecific control of dental plaque “needs to be thorough” and observed that the degree of plaque reduction must be both clinically significant and statistically significant for it to be determined to be effective.

Once again, WhiteHill agrees. In order to be regarded as effective in helping maintain good oral hygiene, an antiplaque product must meet a pre-established degree of reduction in dental plaque determined to be clinically significant as determined using a standardized validated clinical protocol. Contrary to the position of the FDA, WhiteHill maintains such reductions in dental plaque can be affected without the use of antimicrobials. A clinically significant reduction in dental plaque is defined as a reduction that is hygienically significant, *i.e.*, it helps maintain good oral hygiene. The action requested by WhiteHill in Part I of these comments meets these criteria.

B. Dental Plaque is a Natural Component of a Healthy Mouth

All exposed surfaces on the human body are subject to external attack from bacteria and other elements from the environment. To protect themselves, these surfaces form protective layers called “microflora” or “biofilms.” Microflora, whether on exposed or internal surfaces are a:

“dynamic and complex mixture of microbes that have diverse functions including digestion of essential nutrients, maturation of intestinal physiology, stimulation of immune system, systemic effects on blood lipids and the inhibition of harmful bacteria.”³

Germ free surfaces, by contrast, are often subject to “altered mucosal surfaces, poor nutrient absorption, . . . nutrient deficiencies, and . . . impaired host defenses.”⁴

Dental plaque is an important component of the mouth’s natural microflora. This oral biofilm is “part of the natural organic tooth tegument and as such is consistent with health.”⁵ As a result, and as the Subcommittee noted (page 32236), not all dental plaque is pathogenic. Recent advances in the field of oral hygiene have led the scientific community to conclude, for example, that:

“Dental plaque is the biofilm that forms on the surfaces of teeth, and is comprised of a diverse community of bacteria, embedded in a matrix of polymers of microbial and host origin. Plaque develops naturally, and is generally considered of benefit to the host because of its ability to prevent colonization by exogenous (and often pathogenic) micro-organisms.”⁶

³ L.V. McFarland, Normal flora: Diversity and functions, 12 Microbial Ecol. in Health & Disease 193-207 (2000).

⁴ Id.

⁵ N.J. Mordan, et al., The Apical Plaque Border in Health and Disease, *in* (H.N. Newman & M. Wilson, eds.) Dental Plaque Revisited 343-374, at 343 (1999).

⁶ P.D. Marsh, Host defenses and microbial homeostasis: Role of microbial interactions, 68 J. Dent. Res. 1567-1575 (1989) (Special Issue).

Thus, in its normal healthy state, dental plaque is a natural human oral biofilm that exists *in equilibrium* with the oral cavity:

“Once established, the microbial composition of plaque remains relatively stable with time (microbial homeostasis). This stability is not due to metabolic indifference but is a result of a dynamic balance among the component species. This balance involves both antagonistic and synergistic inter-bacterial interactions, where certain organisms are dependent for their persistence on the activity of neighboring species.”⁷

C. Maintaining Dental Plaque Equilibrium Promotes Good Oral Hygiene

Maintenance of this equilibrium is essential to good oral hygiene. As Dr. Marsh has explained, changes in the oral environment “can lead to rejection or enrichment of previously minor components of this oral biofilm, [leading to] clinical changes to host tissues”⁸ Thus, if the microflora is thrown out of balance, it is more likely that a “pathological assault may be initiated.”⁹

One way that the equilibrium may be thrown out of balance is through a “transition” of beneficial plaque to pathogenic plaque. The scientific community has discovered that “a direct relationship exists between the environment and the balance of the resident plaque microflora.”¹⁰ This relationship helps explain the factors that contribute to a “transition of the plaque microflora from having a commensal to a pathogenic relationship with the host.”¹¹

One factor that influences this plaque “transition” is the quantity of plaque in the oral cavity. In general, the more plaque in the oral cavity, the greater the rate of

⁷ P.D. Marsh & D.J. Bradshaw, *Microbial Community Aspects of Dental Plaque*, in (H.N. Newman & M. Wilson, eds.) Dental Plaque Revisited 237-253, at 237 (1999).

⁸ Marsh, *supra* note 6.

⁹ Mordan, *supra* note 5.

¹⁰ Marsh, *supra* note 6.

¹¹ Id.

transition from healthy plaque to pathogenic plaque.¹² The presence of plaque over a baseline of 2.0 on the Turesky Modified Quigley-Hein is considered to be borderline with respect to a healthy level. As a result, it is important to develop techniques to control dental plaque, thus keeping it at a level that is conducive to a balanced microflora equilibrium, in order to help maintain good oral hygiene.

III. Non-Antimicrobial Plaque Reducing Drugs Help Maintain Dental Plaque Equilibrium

Non-antimicrobial plaque reducing drugs are one way to help achieve this goal. By reducing the total amount of dental plaque, these drugs help avoid a transition from healthy plaque into pathogenic plaque. The reduced plaque is then naturally replaced, thus sustaining equilibrium. In this state of equilibrium, the mouth is naturally able to self-regulate. At equilibrium, the mouth presents an infertile ground for the development of oral hygiene problems. Reduction of dental plaque is therefore hygienically significant in that it helps maintain good oral hygiene at the outset.

In this way, non-antimicrobial drugs intended to help maintain good oral hygiene act by affecting the structure or function of the body. Claims such as these clearly fall under the statutory definition of a drug. These claims should therefore be added to the tentative final monograph for OTC antiplaque/antigingivitis drug products and included in an expanded version of the FDA Guidance for Industry.

¹² C.M. Cobb, *Modern Methods for the Mechanical Control of Subgingival Plaque*, in (H.N. Newman & M. Wilson, eds.) Dental Plaque Revisited 457-502, at 427 (1999) (“the quantity, composition and rate of subgingival plaque recolonization is, to some degree, dependent upon supragingival plaque accumulation.”).

structure/function definition of a drug in Section 201(g)(i)(c) of the FD&C Act. As such, these non-antimicrobial anti-plaque reducing agents are to be included in an expanded FDA draft Guidance for Industry.

B. Additional Scientific Support

The authorities cited and quoted in Parts II-IV of these comments represent only a small fraction of the dental literature that supports the reduction of dental plaque in order to help maintain good oral hygiene. A bibliography of additional scientific articles and book chapters supporting the reduction of dental plaque to help maintain good oral hygiene is included as Appendix A to these comments. WhiteHill knows of no dental authorities who contend that reducing dental plaque is unrelated or not helpful in maintaining good oral hygiene.

C. There is no Significant Risk that Reasonable Consumers Will be Mislead

One of the reasons that the Subcommittee gave for declining to recommend claims relating solely to the reduction of plaque was the potential that consumers would be misled into believing that the products involved are therapeutic. According to the Subcommittee (page 32238):

“The claim that a product significantly reduces dental plaque (statistically speaking) may mislead people into thinking that the reduction is therapeutically significant. Thus, people may purchase a product with the mistaken notion that a therapeutic benefit may be derived from its use, instead of seeking effective care for potential signs and symptoms of disease.”

WhiteHill agrees that avoiding consumer confusion is an important consideration in developing any claims for an OTC drug monograph. It is important to distinguish those products that are intended directly to reduce diseases such as gingivitis from those that are not intended directly to affect gingivitis but nonetheless provide important hygienic

benefits through the reduction of dental plaque. The Agency, however, can resolve any potential confusion by explanatory language, without depriving consumers of an important tool for maintaining good oral hygiene.

The claim “helps maintain good oral hygiene” does not in any way suggest therapeutic use. If FDA were to disagree, however, the Agency could, as it has done in the past, simply adjust the claim to avoid consumer confusion. For example, among the acceptable structure/function claims listed in the preamble to FDA’s proposed dietary supplement rule was the claim “Helps maintain a healthy cholesterol level.”¹⁶ The Agency ultimately concluded, however, that this unqualified phrase could confuse consumers because it could be interpreted to refer to high density lipoproteins and thus to the prevention of heart disease. To avoid this potential confusion, FDA decided in the preamble to the final regulation that the appropriate structure/function claim for maintenance of cholesterol levels should be “helps to maintain cholesterol levels that are already within the normal range.”¹⁷

FDA can easily take a similar approach to a structure/function claim for maintenance of good oral hygiene if the Agency deems it necessary to avoid confusion. Indeed, under the recent judicial decisions in Pearson v. Shalala¹⁸ and Whitaker v. Thompson,¹⁹ as now being applied and implemented under the FDA initiatives announced in December 2002²⁰ and July 2003,²¹ FDA is required under the First Amendment to the United States Constitution to permit any truthful and accurate claim

¹⁶ 63 Fed. Reg. 23623, 23626 (April 29, 1998).

¹⁷ 65 Fed. Reg. at 1019.

¹⁸ 164 F.3d 650 (D.C. Cir. 1999), rehearing denied, 172 F.3d 72 (D.C. Cir. 1999)(en banc), 130 F.Supp.2d 105 (D.D.C. 2001), 141 F.Supp.2d 105 (D.D.C. 2001).

¹⁹ 248 F.Supp.2d 1 (D.D.C. 2002).

²⁰ 67 Fed. Reg. 78002 (December 20, 2003).

²¹ 68 Fed. Reg. 41387 (July 11, 2003).

unless the Agency can demonstrate by empirical evidence that there is no way to qualify it in order to make it nonmisleading.

V. The Combination of Polydimethylsiloxane and Poloxamer is Safe and Effective in the Reduction of Dental Plaque

As the Subcommittee recognized in its report (page 32274), the combination of polydimethylsiloxane and poloxamer has been used in a number of different formulations, including sprays, mouthwashes, dentifrices, chewing gum and breath mints. The Subcommittee accepted this combination as Category I for safety, *i.e.*, generally recognized as safe. The Subcommittee did not review this combination (or any other ingredients) for antiplaque effectiveness alone, because of its position that only ingredients that are proved effective against gingivitis should be included in the monograph.

As noted in Part I(B) of these comments, the ratio of the polydimethylsiloxane to the poloxamer varies from 1:100 in mouthwashes to 1:1 in chewing gum. The concentration of the combination ranges from 0.4 percent to 4 percent for liquid and gel emulsions, including toothpaste and other oral health products, and the amount used in products like chewing gum, mints, breath strips, and chewable candies ranges from .01 grams to 0.2 grams per use. Each formulation will vary depending upon the precise characteristics of the product involved. Accordingly, it is essential that the monograph establish a performance test, of the type described above in Part I(D) of these comments, in order to assure consistent effectiveness in the reduction of plaque.

WhiteHill has conducted studies on this combination, using a variety of dosage forms and product formulations. These studies demonstrate that the combination of polydimethylsiloxane and poloxamer can be formulated in a way that achieves the

standard of hygienical significance, *i.e.*, maintenance of good oral hygiene, by a twenty percent reduction in dental plaque, using the type of protocol set forth above in Part I(D) of these comments. In the following paragraphs, we briefly summarize the protocols and results of this testing. The clinical study reports were included as Appendix B to WhiteHill's November 24, 2003 response to the Subcommittee findings.

A. Clinical Research Protocol WHLS - 005

This clinical study examined the effect of frequent daily use of polydimethylsiloxane and poloxamer, in sorbitol-based sugar-free mints, in reducing dental plaque between brushings. The study employed a double-blind crossover design with several different formulations of the test product and a placebo. It followed the protocol described in Section I(D)(1) of these comments, except for a lower number of subjects (n=10).

The subjects were instructed to dissolve one mint at each of six prescribed times (after each meal, between meals, and at bedtime). The results for the three most effective mint formulations, incorporated at 1.5 percent in the mints with polydimethylsiloxane having 0.6×10^6 cs and 2.5×10^6 cs viscosity respectively, were:

Product	PI at Baseline*	PI 48 Hour	< PI Vs. 48 hr Placebo	% Change Vs. 48 hr Placebo	Statistical Significance versus Placebo
Placebo Mint	2.12	2.30	---	---	---
Test Mint A 0.6 X 10 ⁶ cs 1.4 mg PDMS	2.01	1.61	-0.69	-30.0	p < 0.0001
Test Mint B 2.5 X 10 ⁶ cs 1.4 mg PDMS	2.08	1.57	-0.73	-31.7	p < 0.0001
Test Mint C 2.5 X 10 ⁶ cs 0.7 mg PDMS	2.14	1.49	-0.81	-35.2	p < 0.0001

* No statistical difference between baseline readings.

These results clearly demonstrate a statistically and clinically significant difference in the reduction of dental plaque between the placebo mint and all three formulations of test mints. This reduction in dental plaque is sufficient to help maintain good oral hygiene.

B. Clinical Research Protocol WHOTI G-040

This clinical study examined the effect of frequent daily use for four weeks of polydimethylsiloxane and poloxamer in a chewing gum in reducing dental plaque while maintaining normal brushing habits. The study employed a three-arm double-blind crossover design with a test product, a chewing gum placebo, and a mint placebo. It followed the protocol described in Section I(D)(2) of these comments, using 21 subjects.

The subjects were instructed to chew one piece of gum after each meal (three per day). The tested gum formulation contained 1.5 percent of the drug with polydimethylsiloxane having 2.5×10^6 cs viscosity equivalent to 1.4 mg per piece. In addition to a chewing gum placebo arm, a mint control arm was also included in this study as a second placebo to assure that chewing action was not a significant factor. There was no significant difference between the mint control and the placebo gum. There was, however, a significant difference between the mint control and the test gum.

The results, summarized in the table below, clearly demonstrate a statistically and clinically significant difference in the reduction of dental plaque between the placebo gum and the test gum. This reduction in dental plaque is sufficient to help maintain good oral hygiene:

Product	Initial PI Baseline	Final PI Day 28	< PI Vs. 28 day Placebo	% Change Vs. 28 day Placebo	Statistical Significance <i>versus</i> Placebo
Placebo Gum	2.18	2.25	---	---	---
Test Gum 1.5% emulsion 1.4 mg PDMS	2.18	1.48	0.77	34.2	p < 0.0001

C. Clinical Research Protocol WHOTI G-041

This clinical study was a repeat of WHOTI G-40, described above, using the same placebo gum and test gum formulations. A mint control was not employed in the G-041 study. The results from this study, summarized in the table below, confirm the findings from the WHOTI G-40 trial of statistical and clinical significance in helping maintain good oral hygiene:

Product	Initial PI Baseline	Final PI Day 28	< PI Vs. 28 day Placebo	% Change Vs. 28 day Placebo	Statistical Significance <i>versus</i> Placebo
Placebo Gum	2.28	2.28	---	---	---
Test Gum 1.5% emulsion 1.4 mg PDMS	2.18	1.40	0.88	38.6	p < 0.0001

D. Rawhide Study in Dogs

A rawhide chew-treat study examining the effect of polydimethylsiloxane and poloxamer in reducing dental plaque in dogs was published in the Proceeding of the 1994 World Veterinary Dental Congress.²² Rawhide is the nearest animal equivalent to human chewing gum. The published article does not chemically identify WhiteHill's drug because of sponsor trade secret concerns that existed in 1994. Instead, the study sponsor accurately described the drug by function as one which:

"interrupts the formation of plaque by coating the teeth with a smooth thin film that prevents materials from adhering to tooth surfaces."

The rawhide chew treat study used a protocol similar to the human chewing gum studies described in Section I(D)(2) of these comments, using 18 dogs. The dogs were divided randomly into three groups of six dogs each. The first group received no treatment, the

²² M.L. Sharp, et. al., A test method to evaluate the efficacy of a formulation on plaque, tartar and mouth odor in dogs, Proc. World Vet. Dent. Congress 82-84 (1994).

second group received untreated rawhide (placebo), and the third group received treated rawhide. The coated treats contained approximately 200 mg of the drug per chip.

The dogs were scored for plaque using an animal-suitable modification which combined the Silness-Loe Plaque Index (1964) for the low scores of 0-3 and the Turesky Modified Quigley-Hein Plaque Index for scores of 4-5. After an initial prophylaxis to reduce plaque to zero, dogs in groups two and three were given three of the assigned treats per day and plaque scores were evaluated bi-weekly for 24 weeks. The authors summarized the results of the study:

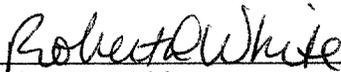
"plaque and tartar build-up on cleaned teeth was significantly less for dogs chewing coated treats than for dogs offered placebo treats, the reduction ranging from 24-32% for plaque"

These results clearly demonstrate a statistically and clinically significant difference in the reduction of dental plaque between the placebo treat and the coated treat. This reduction in dental plaque is sufficient to help maintain good oral hygiene.

In light of the results of these human and animal studies, FDA should: (a) accept the combination of polydimethylsiloxane and poloxamer as one of the safe and effective antiplaque ingredients that will be listed under the new section of the monograph requested in Part I(B) of these comments, and (b) adapt an expanded version of the draft Guidance for Industry to include antiplaque ingredients with no gingivitis endpoint as a drug that maintains good oral hygiene.

VI. Conclusion

For the reasons set forth above, WhiteHill requests that FDA recognize that the combination of polydimethylsiloxane and poloxamer is Category I to help maintain good oral hygiene, in accordance with the conditions established in Part I of these comments.



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