

Acceptance Program
Guidelines

Home-Use Tooth Stain Removal Products

Council on Scientific Affairs

Home-Use Tooth Stain Removal Products

Purpose:

The purpose of these guidelines is to determine the safety and efficacy of home-use tooth stain removal products that involve any non-bleaching ingredient or process for extra-coronal application that increases the lightness of natural teeth by removal of extrinsic tooth stains.

Scope:

These guidelines apply to all home-use tooth stain removal systems utilizing any non-bleaching ingredient or process designed for extra-coronal application which removes extrinsic tooth stains in order to improve the esthetic appearance of natural teeth. Products that alter intrinsic tooth color are covered under the Guidelines for Over the Counter Home-Use Tooth Bleaching Products and the Guidelines for Dentist Dispensed Home-Use Bleaching Products. Professional in-office bleaching products are covered under the Guidelines for In-Office Bleaching Products.

I. SUBMISSION DIRECTIONS

1. General Information

- A Submissions should be sent to the Council Office:
Director, Product Evaluations
American Dental Association
Council on Scientific Affairs
211 East Chicago Avenue
Chicago, Illinois 60611-2678

- B Submissions should be sent in triplicate along with a market sample of the product (i.e., packaged as marketed). The Council agrees to return the product sample within six months if requested. If possible the submission should be less than 200 pages exclusive of appendices.

- C A manufacturer is advised that the review process is complex. Typically, notification of Council action may be expected in 90 to 150 days from the receipt of a complete submission by the Council. More time may be required if additional information or clarification is needed from the manufacturer.

- D When a product is classified as "Accepted" the classification is valid for three years. The Council upon request will consider renewal of the classification by the manufacturer.

- E Classification of a product under the Acceptance Program is subject to the conditions stated in the contract entitled "Agreement Governing Use of ADA Seal of Acceptance".

2. Arrangement of a Submission

- A The submission is to be divided into sections and arranged in order as indicated in part II. Sections to be identified by tabs are designated by *.

II. INFORMATION TO BE SUBMITTED

1. Cover Page

- A Name of company
- B Product name

*2. Table of Contents

*3. Company Information

- A Name of company (to be used in official list of Accepted Products)
- B Address (to be used in listing)
- C Phone number (to be used in listing)
- D Fax number
- E Email address and Internet address (if available)
- F Names of owners, officers, and other individuals authorized to furnish information to the Council and represent the firm in dealing with the Council. (Foreign manufacturers must have an office or branch located in the United States and the product must be available for purchase in the United States).
- G Names and qualifications of scientific personnel responsible for formulation and testing of the product in its manufacturing process.

*4. Summary of Submission

Comprehensive summary of the information submitted on safety and effectiveness of home-use tooth stain removal products.

*5. Product Information

- A Name of product (to be used in listing).
- B Evidence of FDA approval to market¹, if applicable (e.g., 510 (k) letter, pre-market approval [PMA], NDA.)
- C Claims of efficacy and safety.
 - (i) List of claims of efficacy and safety. All claims of safety and efficacy such as whitening², brightening³, and lightening⁴ must be documented, including all claims in advertising and promotional materials.
 - (ii) The studies (or parts of studies) that provide documentation for each claim must be identified.
 - (iii) Advertisements must avoid disparagement of other tooth stain removal systems.
- D Patent title(s) and patent number(s) relating to the product.

¹ This requirement may be waived by the Council during the evaluation period. Evidence must be provided prior to use of the ADA Seal if the product is Accepted.

² Whitening is defined as the process that results in the material becoming similar in color to a preferred or standard white.

³ Brightening is defined as the process that results in a material appearing to reflect either diffusely or specularly, more light.

⁴ Lightening is defined as the process that results in the material reflecting diffusely a greater amount of the incident light.

- E Product composition and mode of application
 - F Instructions including indications and contraindications for use
All instructions for the use of home-use tooth stain removal system, including any adjunctive materials (e.g., fluoride gels), should be clearly defined as to method of application, exposure time, and other related techniques. This recommended procedure for use, as defined in the instructions, is the one that is to be tested in laboratory and clinical evaluations for the purposes of the current guidelines. Any substantial departures from these instructions would represent a different home-use tooth stain removal system and would require separate evaluation.
 - G Labeling
 - H Packaging
 - I Promotional materials
- *6. **Procedures for the Manufacturing of the Product**
Describe the quality control procedures applied to the manufacturing of the product. This should include the quality control tests used during processing and on the finished product and assurance that the product meets good manufacturing procedures.
- *7. **Laboratory Evaluation**
Supply one copy of all available physical and chemical property information developed in laboratory studies that is published or similar materials that might be predictive of clinical behavior.

The following tests should be conducted on extracted human teeth that have been stored in appropriate media, such as 2% sodium azide, and not subject to any conditions that would alter their general properties. Most likely the teeth would be extracted third molars; however, they should be erupted for at least a year. Their enamel is considered an acceptable representative of the enamel for the facial surfaces of anterior teeth, if anterior teeth are not available.

A Enamel hardness testing

Tooth stain removal systems could potentially damage dental enamel or dentin under extreme conditions of use. To insure that no substantial changes in the morphology and/or properties of enamel occurs, enamel hardness must be evaluated before and after treatment according to the product's usage instructions. The average Knoop hardness shall be determined by applying a 0.490 N (50 gf) load in accordance with ASTM C 1326. When using this ASTM test method, special attention should be given to the following test parameters: specimen minimum thickness, specimen surface finish, specimen leveling, and spacing of indentations. Furthermore, guidance on the acceptability of indentations shall be adhered to along with the instructions for measurement of indentations. The average Knoop hardness number of ten acceptable indentations before and ten acceptable indentations after treatment shall be compared. These indentations shall be made on the same region on the facial surface of an extracted tooth that has been stored in an appropriate solution, such as 2% sodium azide (note that ASTM C 1326 requirements for minimum spacing of indentations need to be followed). There should be no statistically different difference in the mean hardness values before and after treatment at the $p < 0.05$ level for a t-test comparison. Test reporting shall comply with the "Report" section of ASTM C 1326.

B Enamel morphology changes

Tooth stain removal systems may potentially produce interactions such as dissolution of prism material. For example, these interactions may produce changes in tooth surface roughness. Enamel abrasivity shall meet the

requirements of enamel abrasion in ISO 11609:1995. Evidence must be presented that the product does not degrade the surface of the treated enamel and increase its susceptibility to caries demineralization and erosion.

c Restorative materials changes

Resin-based and glass-ionomer restorative materials have the potential to experience loss of physical integrity after exposure to stain removal systems. On the other hand, metals and ceramics have a very low potential for reacting with stain removal systems. The verification of physical properties for resin-based and glass ionomer restoratives should be done by comparison of transverse rupture strength (TRS) and transverse modulus (TM) before and after exposure to the stain removal system for a period of time simulating clinical use as recommended by the manufacturer. The materials tested should be one brand of microfill composite resin, one conventional glass ionomer cement, and one resin-modified glass ionomer cement. For acceptability, the TRS and TM must not differ between before and after treatment with the stain removal system. The sample dimensions, fabrication methods and test methods from ADA Specification No. 27 for Polymer-Based Filling, Restorative, and Luting Materials should be used to determine TRS and TM. Acceptance will be contingent upon achieving statistically similar means of TRS and TM from ten samples tested before and after exposure to the stain removal system. Similarity of means will be verified by t-test at a significance level of $p < 0.05$ and reported as the group means, standard deviations, and p value for the t-test.

D Kinetics of active ingredient release

The release kinetics of all active ingredients (if applicable) during the recommended use (i.e. amount of active ingredient recovered, intraorally, for at least four different time periods) shall be evaluated.

***8. Toxicological Evaluation**

Where appropriate, products are required to meet the safety requirements detailed in *Guidelines for the Acceptance of Peroxide-Containing Oral Hygiene Products*. (see V. References, No. 1).

***9. Clinical Evaluation**

Safety shall be demonstrated by the absence of irreversible side effects resulting from the use of the product. Human efficacy shall be demonstrated using at least one appropriate index for measuring stain removal.

The following guidelines are for the design and conduct of clinical studies to provide evidence of safety and efficacy. Additional information concerning clinical trials and clinical trial reporting can be obtained from the Council's *Guidelines for Clinical Trial Protocols* (see V. References, No. 4). Manufacturers are encouraged to submit their clinical protocols to the Council for review prior to the start of the clinical studies. The information indicated below is applicable to each independent clinical study.

A Trials

At least two independent⁵ double blind clinical trials are required, each at a different site. All sponsored clinical studies evaluating the product in question should be identified at the time of filing.

B Observation times

For those products with a prescribed treatment period, an observation immediately post-treatment is required. For all products, observations are required at 3 weeks and 6 weeks following initiation of treatment.

After subject screening, selection and initial instruction the stain removal system will be used for a test period

⁵ Different sites, different investigators, and different populations. One investigation may be conducted by the companies' research department.

recommended in the instructions for use. Materials and subject logs will be collected at the end of the test period during the recall.

C Subject Selection

All subjects should have naturally induced stain, no obvious signs of periodontal disease or untreated dental caries, at least four maxillary anterior teeth that would qualify for the tooth stain removal trial, and be in good physical health with no medical problems that would contraindicate participation in the clinical trial. Subjects should be screened for potential participation in the trial and the screening pool should be examined for balance in terms of gender and broad age distribution. Subject population should be indicative of those for whom the product is intended.

D Subjects

A typical clinical trial of this type generally involves at least 25 subjects in each group, experimental and control. The control should be the product not containing the active agent(s). For toothpastes, the control should be an ADA Accepted non-whitening toothpaste with abrasive. Other suitable controls will be considered by the Council. Any teeth containing restorations that may be exposed to the test agent during the trial, may be excluded because of potential problems or biases caused by the existing restorations. Subjects should not have participated in tooth stain removal trials for at least 3 months. Subjects with dentinal sensitivity should be excluded or the sensitivity should be resolved before the start of the study.

- (i) Teeth per subject: At least four teeth per subject (maxillary or mandibular central and lateral incisors) will be evaluated.
- (ii) Subject distribution by gender and age: The subject pool should have a relatively even distribution of subjects of both genders (40% to 60% male or female) and should have some representatives of a wide range of ages.

E Stain removal measurement methods

Stain removal on teeth should be measured using at least one of the following methods: i) color measurement devices such as colorimeters or spectrophotometers; ii) special color matching scales (e.g., porcelain shade guides, custom shade guides); or iii) stain removal indices (e.g. Lobene Stain Index). Justification of the evaluation method must be provided. Reliability of method must also be assessed.

F Evaluation periods

For each group, teeth must be evaluated in a natural state of hydration at the start of the test period, end of the test period (for products with a prescribed treatment period), 3 and 6 weeks post initiation of product use. Test periods may vary depending on the nature of the application regime. Reports summarizing the clinical information at the following recall periods in the studies should be submitted for review by the ADA Council on Scientific Affairs.

- (i) Start of testing period (0 weeks).
- (ii) End of test period (for products with a prescribed treatment period).
- (iii) 3 weeks post-initiation of treatment (if no prescribed treatment period).
- (iv) 6 weeks post-initiation of treatment (if no prescribed treatment period).

G Clinical evaluation procedures and records

Document the procedures, methods of clinical evaluator training for compliance with the procedures, and methods of recording the clinical evaluation data.

- (i) Clinical evaluators: Record the identification of the operator for each clinical evaluation for future reference to consider the potential for operator effects on the evaluations. Whenever possible, the same clinical evaluator should see the same subject during all of the recalls.

- (a) Evaluator training and retraining (when using shade guides or stain indices): All evaluators must establish prior to participation in the clinical trial that they meet a minimum of 85% consensus with a standard evaluation scale for the evaluation of interest. It is expected that before each recall phase of the clinical trial that each evaluator be calibrated once again using the standardized procedure. All of the details of the standardized procedure must be described for any reports and the outcomes of the standardization should be reported. Any examiner failing the standardization procedure may repeat the process until a level of 85% consensus is achieved.
 - (b) Inter-evaluator effects (when using shade guides or stain indices): For each recall evaluation, the results of the clinical evaluations shall be statistically analyzed ($\alpha \leq 0.05$) by evaluator to determine if any evaluators are different from the group.
 - (c) Intra-evaluator effects (when using shade guides or stain indices): For the first recall evaluation, the results of the clinical evaluations shall be reported by two clinical evaluators for at least half of all evaluations with at least an 85% consensus of results. This will function to confirm that the standardization procedure is in fact working.
- (ii) Stain removal measurement procedures
 - (a) Controlled lighting conditions: The lighting conditions must be carefully controlled to guarantee that full spectrum natural light is available for measurements, that other light is excluded, and that strong absorbers (such as dark colored walls or equipment) are not present that could alter the color being observed. All measurements should be made under the same lighting conditions for each observation period.
 - (b) Tooth color or stain removal record keeping: All of the variables of the measurement procedures should be recorded. At each evaluation time, information should be collected on the evaluator(s), time of day, procedures for producing full spectrum natural lighting conditions, methods of excluding other light sources, the operatory location, and date.
 - (iii) Gingival health measurement procedures: Measurements on, at a minimum, the Ramjford teeth, at baseline, at the start of the test phase, at the end of test phase (for products with prescribed treatment period), and at the other recall periods (see II.9.F) should be made for gingival health, e.g. Loe and Silness Gingival Index and plaque using standard procedures, e.g. Silness and Löe Plaque Index.
 - (iv) Oral Tissues
Oral soft and hard tissues must be evaluated for adverse effects at each examination period and these results reported.
 - (v) Adverse Effects
All adverse effects should be reported including altered oral sensations, e.g. burning mouth, altered taste, and tooth sensitivity for each observation period. Restorations should also be evaluated for adverse effects.
10. **Comprehensive bibliography**
Appropriate references should be included to document statements or comparisons made in the report to the ADA Council on Scientific Affairs.
11. **Copies of most significant articles**
In cases in which the stain removal measurement used in the clinical trial is substantially different from those

described in this document, then significant articles describing the use, validation, calibration, and controls should be submitted with all reports to the ADA Council on Scientific Affairs.

12. **Appendices**

Detailed descriptions of test evaluation methods and any other defined areas should be included with any reports submitted to the ADA Council on Scientific Affairs.

III. ACCEPTANCE CRITERIA

1. Establishment of safety

Safety shall first be determined by favorable performance of the product in laboratory tests before clinical trials are initiated (see section II.8). Documentation of non-persistent hypersensitivity, gingival health, and adverse effects during all tests in the clinical trial for the time intervals and at the response levels listed below shall be required.

2. Establishment of efficacy

Efficacy shall be established by favorable performance of the product in laboratory tests and successful documentation of stain removal in the clinical trial for the time intervals and at the response levels listed below. The product must also demonstrate a statistically significant difference when comparing the change from baseline to a subsequent time point vs. that change for the placebo control

A Evaluation periods

Clinical information shall be collected at the times listed below. The percentage of subjects at each recall must be recorded along with the reasons for the subject dropout. Data must be based on the recall levels as indicated below.

- (i) Start of testing period.
- (ii) End of testing period (for products with a prescribed treatment period (PPTP)).
- (iii) 3 weeks post-initiation of treatment.
- (iv) 6 weeks post-initiation of treatment.

B Efficacy levels

For the test product the recalled teeth in "each independent clinical study" must demonstrate clinical evidence equal to or exceeding the following limits compared to the control (see Section II. 9.E):

	<i>Color Change</i> <i>in color change units (ccu)</i>	<i>Stain Index Decrease</i>
(i) Start of test	---	---
(ii) End of test period (PPTP)	$75\% \geq 2 \text{ ccu}$	$75\% > 0.5u$
(iii) 3 weeks post-initiation of treatment	$75\% \geq 2\text{ccu}$	$75\% > 0.5u$
(iv) 6 weeks post-initiation of treatment	$75\% \geq 2 \text{ ccu}$	$75\% > 0.5u$

2 ccu = either a change ≥ 2 steps using a 16 step Vita Pan Classical value ordered shade guide or a change of $\geq 2.0 \Delta E$ units using the $L^*a^*b^*$ system comparing post-treatment scores to pre-treatment scores

1 u = 1 unit decrease in the severity and coverage of stain based on the Lobene Stain Index (Reference 2) comparing post-treatment scores with pre-treatment scores

IV. STATEMENT

To be used for products classified under these guidelines including qualifiers.

"The ADA Council on Scientific Affairs Acceptance of (Product Name) is based on its finding that it effectively removes surface stains when used according to the manufacturer's instructions."

V. REFERENCES

1. American Dental Association Guidelines for the Acceptance of Peroxide-Containing Oral Hygiene Products, Council on Dental Therapeutics, American Dental Association. JADA 1994; 125:1140-1142.
2. R. R. Lobene, Effect of Dentifrices on Tooth Stains with Controlled Brushing. JADA 1968; 77:849-855.
3. ASTM International Standard C 1326:1999, Standard Test Method for Knoop Indentation Hardness of Advanced Ceramics. Conshohocken, PA: ASTM International.
4. ADA Council on Scientific Affairs, ADA Acceptance Program Guidelines for Clinical Trial Protocols. Chicago: American Dental Association.



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