Acceptance Program Requirements

Products to Help Prevent or Reduce Enamel Erosion

Acceptance Program Requirements

This document outlines specific category requirements. Please also refer to the General Guidelines for Participation in the ADA Seal of Acceptance Program.

Category:	Products to Help Prevent or Reduce Enamel Erosion
Purpose:	The Acceptance Program applies to over-the-counter dental products for which safety and efficacy has been established by laboratory and/or clinical evaluations where appropriate. Accordingly, the purpose of these requirements is to provide a structure upon which products intended to help prevent or reduce enamel erosion from dietary acids can be considered for ADA Acceptance.
Scope:	These requirements apply to help prevent or reduce enamel erosion directly from dietary acids. Products containing fluoride and/or other active ingredients must also satisfy additional category requirements.
Notice Regarding Submission of Copyrighted Materials:	To make the review of submissions to the ADA Acceptance Program as efficient as possible, the Council on Scientific Affairs provides copies of submitted materials to Council members and consultant reviewers, and also posts submitted materials to an area of the ADA's web site the access to which is restricted to Council members and staff. By making a submission, you are representing and warranting to the Council on Scientific Affairs and the ADA that you have obtained sufficient permission(s) from the copyright owner(s) of any copyrighted material included with your submission to allow for the publication and distribution of that material by the ADA as described above, and agree to indemnify and hold ADA harmless from any and all claims arising from such publication or distribution. Questions can be directed to adaseal@ada.org.

1. SEAL STATEMENT

The following statement applies to products approved under the below-listed criteria:

> "The ADA Council on Scientific Affairs' Acceptance of (Product Name) is based on its finding that the product is safe and has shown efficacy in helping to prevent or reduce enamel erosion from dietary acids, when used as directed."

Format for product packaging:

- Helps prevent or reduce enamel erosion from dietary acids

2. SUBMISSION DIRECTIONS

A. Submissions are to be sent in electronic format (email) to adaseal@ada.org. Additional instructions will be provided regarding shipment of necessary samples.

B. The submission fee is a one-time, non-refundable fee and is required before review begins. Maintenance fees are billed to the company in January of every year.

C. The review timeline for new submissions is typically 4-6 weeks after all materials have been received. The decision to award the ADA Seal to a new product is made by the Council on Scientific Affairs. Family submissions may take anywhere from 2-4 weeks to review. Eligibility criteria for Family Submissions are outlined in the Guidelines for Participation in the ADA Seal of Acceptance Program.

Note: This is an estimated timeline. Extended review time may be required if additional information or clarification is needed from the manufacturer.

D. When a product is classified as "Accepted" and is awarded the ADA Seal of Acceptance, the Acceptance period is five years. Manufacturers will be contacted approximately six months before the expiration of the current Acceptance period to complete the requirements for the next five-year Acceptance period.

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

F. Guidelines for the design and conduct of clinical studies are provided in Appendix I. Manufacturers interested in seeking the ADA Seal of Acceptance are encouraged to submit their clinical protocols to the Council for review prior to the start of clinical studies.

3. SUBMISSION MATERIALS

All submissions must include the following information based on product type and comply with the 'General Criteria for Acceptance' described in the Guidelines for Participation in the ADA Seal of Acceptance Program.

A. Product Information

i. Name of product(s)

ii. Name of company

iii. FDA Documentation

a) FDA registration and product listing must be provided.

b) Evidence of FDA approval to market, if applicable (e.g., 510 (k) letter, pre-market approval, NDA/Evidence of FDA registration).

iv. Product Claims

a) Products approved under these category requirements will receive the following Seal bullet claim: helps prevent or reduce enamel erosion from dietary acids. Data required to substantiate efficacy towards the Seal bullet claim is explained in Section C below. ***Please provide a list of all additional safety and efficacy claims beyond the Seal bullet claim. These claims should follow the ADA Advertising Standards and must undergo review and approval by the Council on Scientific Affairs before they can be included on product packaging.*** Substantiation for any health benefit claims, outside of the Seal bullet claims, must be provided through clinical and/or laboratory data specific to the product and is not addressed in Section C below. Whether clinical or laboratory data is required depends on the nature of the claim. For any questions regarding claim substantiation, please contact the ADA Seal Program.

b) NOTE: Non-fluoride products submitted under this category alone cannot include a Seal bullet claim for cavity prevention. However, if the product includes a cavity prevention claim beyond the Seal bullet claim anywhere on the packaging, evidence of efficacy and safety in the reduction of dental caries must be provided. At least one clinical trial will be required. Please refer to the Clinical Protocol Guidelines for Caries in the ADA Seal Fluoride Dentifrice Category Requirements.

v. Product Specifications

a) Chemical composition or components of the product and purpose of the various ingredients. To facilitate review, submitting the chemical composition, concentration, and purpose in tabular form is recommended.

b) Material Safety Data Sheet (MSDS) (if applicable)

c) Design of the product (if applicable)

vi. Product Manufacturing

a) Describe or list the quality procedures for manufacturing or testing of the product which demonstrate compliance with Good Manufacturing Practices.

b) Certification of Good Manufacturing Practices can also be provided.

vii. Product Instructions

a) Include detailed instructions for product use.

b) Include indications and contraindications for use, warnings, etc.

viii. Product Labeling/Packaging

a) All labeling/packaging should follow the ADA Advertising Standards and must be approved by the Council on Scientific Affairs before use. Companies may submit draft copy for approval. See iv. Product Claims above.

ix. Product Samples

a) Submission requires three samples, one from three different production lots for analysis by the ADA Laboratories.

B. Safety Data

i. Evidence must be provided that the components of the product are safe for use in the oral cavity When appropriate, standard toxicological, mutagenic, and/or carcinogenic testing may be required. Compliance with applicable FDA standards should be provided (where appropriate).

ii. Safety must be demonstrated in two, independent clinical studies. If the product contains ingredients not on the generally recognized as safe (GRAS) list, at least one six month clinical safety study will be required. See Appendix for details regarding clinical protocol guidelines.

iii. Safety must also be demonstrated by the absence of irreversible side effects resulting from the use of the product. Documentation of adverse effects during all tests in the clinical trial are required.

iv. All submitted dentifrices must meet ANSI/ADA Standard No. 130 or ISO 11609, Dentistry - Dentifrices - Requirements, Test Methods and Marking.

C. Efficacy Data

i. Supply one copy of all available physical and chemical property information developed in laboratory studies or similar materials that might be predictive of clinical use/behavior.

ii. Efficacy must be established by two, independent clinical studies assessing the ability of the product to help prevent or reduce enamel erosion from dietary acids. At lease one study must demonstrate a statistically significant improvement when comparing measurements of surface loss from study baseline to endpoint vs. that change for an appropriate control. The second study may follow a similar protocol, or may demonstrate a statistically significant improvement of the surface hardness of demineralized enamel following treatment vs. the control. A detailed description of the methodologies, including validation, calibration and controls, will be required for submission to the Council for review. See Appendix for details regarding clinical protocol guidelines.

iii. For products that also contain active agents for other purposes relevant and additional ADA Acceptance Program Requirements must also be satisfied, as appropriate.

D. Supporting Literature: Copies of the most significant articles or supporting literature demonstrating safety or efficacy of the product should be provided, where applicable.

4. REFERENCES

The following references were used in the development of these requirements and can be consulted for a more detailed discussion:

- ANSI/ADA Standard No. 130 Dentifrices – Requirements, Test Methods and Marking 2020.
- ISO 11609:2017, Dentistry - Dentifrices - Requirements, Test Methods and Marking.
- ADA Advertising Standards: http://www.ada.org/publications/advertising-standards
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Appendix
Clinical Protocol Guidelines for Products that Help Prevent or Reduce Enamel Erosion

The following guidelines are for the design and conduct of clinical studies for the evaluation of the safety and efficacy of products to prevent or reduce enamel erosion. The study duration and design guidelines were developed for studies utilizing surface loss measurements to demonstrate efficacy. For studies utilizing surface microhardness measurements, the Council recognizes that alternative protocols may be appropriate. Manufacturers are encouraged to submit their clinical protocols to the Council for review prior to the start of the clinical studies.

Sample Size
A sufficient number of subjects per treatment group should be enrolled to ensure that appropriate statistical tests can be performed.

Subject Selection
Each subject will have a complete oral cavity examination to determine eligibility for the study. Subjects should have no obvious signs of periodontal disease, dental erosion, or untreated dental caries and be in good physical health with no medical problems, such as acid reflux, that would contraindicate participation in the clinical study. Subjects should be screened for potential participation in the study 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. For each subject, stimulated and unstimulated salivary flow rates, as well as the salivary pH, should be measured and recorded as normal or approximately neutral, respectively, for each subject. Subjects should not be taking medication which alters salivary flow and an adequate period of cessation of medication should be considered. Subjects should be provided with ADA-Accepted products to maintain regular oral hygiene; including a toothbrush, a fluoride toothpaste, and an interdental cleaner. Subjects must refrain from the use of oral health products other than those provided, as well as consuming food and drink (other than sips of water) between treatment and challenge periods. Other criteria for inclusion and/or exclusion of subjects must be provided.

Study Duration
The study shall be conducted as a cross-over or parallel design. Both the control and test products should be used for a minimum of 10 days of treatment. A washout period of a minimum of one week should be employed between test and control products.

Study Design
The test product should be compared with an appropriate control. Masked studies are required. *In situ* protocol utilizing a well fitting and consistently positioned removeable intraoral appliance bearing at least two enamel specimens (human or bovine is acceptable) is required. Specimens must be carefully cleaned to eliminate soft tissue, stored in a disinfecting agent, and sterilized prior to use. The appliance should be worn and conditioned in the oral environment for at least 2 hours before product use in order to form the salivary pellicle. Intraoral appliances should be removed during specified times for eating, drinking, and brushing teeth.

The frequency of use of the product should be representative of actual use of the product in practice. For dentifrices, the Council recommends two, two minute treatments per day utilizing a toothpaste slurry (1:3 dilution in distilled water (w/w), for example). Each treatment should be followed by a minimum of two, five minute *in vitro* challenges in 1% citric acid at pH 3.8, or similar, at room temperature using agitation (ie. sonication). At least one hour should exist between treatment and each acid challenge steps, as well as between treatment/challenge cycles.

Alternative study designs, especially in studies utilizing surface microhardness measurements, may be acceptable and should be submitted to the Council for review.

Safety Assessments
Safety must be evaluated for at least the length of time consistent with the directed treatment period and

acceptance is contingent upon demonstrating the absence of irreversible side effects resulting from the use of the product.

Adverse Events
All adverse events should be reported for each observation period. Restorations should also be evaluated for adverse events.

Effect on Oral Tissues
Evidence that the product does not adversely affect oral soft issues should be provided. Subjects should be examined in the course of the study for mucosal irritation or inflammation.

Efficacy Assessments
Surface loss (or surface microhardness) measurements shall be determined at baseline and endpoint of each treatment group.

Statistical Analysis
Acceptance is contingent upon achieving a statistically significant difference in surface loss (or surface microhardness) from baseline in comparison to that of the control. Mean group scores will be compared at baseline and when treatment is complete. If more than two groups are being evaluated, appropriate multiple comparison tests should be used. The basis for statistical sizing must be provided in the protocol.

Where appropriate, a non-parametric test will be used to assess safety evaluation data (normal vs. abnormal).