Acceptance Program Requirements

Products for the Temporary Relief of Dry Mouth

ADA American Dental Association®
Council on Scientific Affairs

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 for the Temporary Relief of Dry Mouth
Purpose:	The Acceptance Program applies to over-the-counter dental products for which safety and usefulness 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 for the relief of dry mouth can be considered for ADA Acceptance.
Scope:	These requirements apply to products that are useful in the temporary relief of dry mouth. Products evaluated using these requirements relieve symptoms associated with dry mouth through moisturization and not solely by physical stimulation to increase salivary flow. Products with therapeutic benefits that fall under the scope of other categories of the Acceptance Program must also satisfy those 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 toothbrushes 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 moisturizing the mouth to temporarily relieve dry mouth, when used as directed."

Format for product packaging:

- Helps moisturize to relieve dry mouth

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 moisturize to relieve dry mouth. 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.

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, as well as the Generally Recognized as Safe (GRAS) list should be provided (where appropriate). If the product contains ingredients not on the generally recognized as safe (GRAS) list, additional safety studies may be required. See Appendix for details.

ii. Safety shall also be demonstrated by the absence of irreversible side effects resulting from the use of the product. Documentation of adverse events during all phases of clinical or laboratory testing are required.

iii. The product must have a pH between 5.5 – 10 demonstrated via laboratory testing.

iv. All submitted oral rinses must meet ANSI/ADA Standard No. 116 or ISO 16408, Dentistry – Oral Care Products – Oral rinses.

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 shall be demonstrated by two, independent clinical studies of no less than one week assessing the ability of the product to help relieve dry mouth symptoms compared to an appropriate control. Claims of other lengths of time for product effectiveness must be supported by accompanying data.

iii. Additional studies, such as in-vitro moisture retention assays, may also be submitted in support of the product. Dermal phase meters or other moisture retention instrumentation available on the market as well as an appropriate testing substrate should be utilized. Manufacturers are encouraged to submit a detailed description of such methodologies, including validation, calibration and controls, to the Council for review.

iv. 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:

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- ANSI/ADA Standard No. 116 – Oral Rinses 2020
- ISO 16408:2015, Dentistry – Oral Care Products – Oral Rinses
- ADA Advertising Standards: https://www.ada.org/publications/advertising-standards

Appendix
Clinical Protocol Guidelines for the Temporary Relief of Dry Mouth

The following guidelines are given for the design and conduct of clinical studies to provide evidence of safety and efficacy for products intended to moisturize the mouth to relieve dry mouth symptoms. Clinical effectiveness shall be demonstrated by a perceived improvement in test subjects. Manufacturers are encouraged to submit their clinical protocols to the Council for review prior to the start of clinical studies.

Sample Size
A sufficient number of subjects should be enrolled in the study to ensure that appropriate statistical tests can be performed. The Council recommends that a minimum of 30 subjects per treatment group complete the study.

Subject Selection
Subjects should be screened for potential participation in the study using a dry mouth inventory questionnaire to assess severity of reported dry mouth in each subject. Each subject will have a complete oral examination to determine eligibility for the study and must be at least 18 years old. The screening pools should be balanced in test and control groups in terms of gender and age distribution. The subject populations should be indicative of those for whom the product is intended, which may include subjects with drug-induced xerostomia, Sjogren's syndrome where the autoimmune condition impacts salivary flow and head and neck cancer patients where salivary flow is compromised due to chemotherapy/radiation.

Study exclusion criteria should apply to subjects who are pregnant and/or currently breast feeding; allergies and idiosyncratic responses to product ingredients; eating disorders; recent history of substance abuse; participation in other clinical studies within 14 days of screening; or periodontal surgery or orthodontic treatment in the preceding three months. Other criteria for inclusion/exclusion of subjects must be provided.

Study Duration
The Council recommends that two clinical studies of no less than one week are necessary showing safety and effectiveness of the product. Claims of other lengths of time for product effectiveness must be supported by accompanying data.

Study Design
The clinical study should be double-blind, with random selection of subjects using either a parallel or crossover design. The frequency of use of the product should be representative of actual use of the product in practice and the user should be instructed in the proper use of the product, but not necessarily supervised. Subjects should be provided with ADA-Accepted products to maintain regular oral hygiene including a toothbrush, a fluoride toothpaste lacking claims to relieve dry mouth symptoms, and an interdental cleaner.

The test product should be compared to an appropriate control. Studies must report all treatment groups and an attempt should be made to assess the level of compliance of the subjects in the study. Masked studies are required. It is recommended to submit draft protocols to the Council for review before that start of the clinical trial if any aspect of the study design is in question.

Safety Assessments
Effect on oral soft tissues
Evidence of the lack of effects on oral soft tissues should be provided. Observation of soft tissues should be conducted in patients during the study for the development of abnormal conditions, such as candidiasis, oral ulcerations, or other manifestations of opportunistic microorganisms that proliferate and may lead to secondary mucosal lesions.

Effect on teeth
Evidence of the lack of effects of the product on teeth should be provided.

Effect on dental restorations
Evidence of the lack of adverse effects on dental restorations (e.g. composite resins, porcelain, etc.) should be provided.

Toxicology
Information submitted for potential effects of agents in the products shall include assessments of possible toxic effects of these agent(s) or adverse effects of the product formulation. These should include standard toxicological profiles depending on the particular product.

Patient perceived adverse events
Data should be provided on the product, if any, regarding patient reports of burning sensations, changes in taste, changes or lack thereof in salivary flow, dry mouth symptoms, or other characteristics that may be uniquely due to the product.

Efficacy Assessments
Efficacy shall be demonstrated by achieving a statistically significant reduction of dry mouth symptoms from baseline in comparison to that of an appropriate control. This should be demonstrated through subject response questionnaires administered at different time points throughout the length of the study as well as post-treatment using a visual analog scale (VAS) or other subject response forms.

Mean group values 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. Information to be provided includes expected examiner variance, the targeted alpha and beta values, the estimated drop-out rate, and the targeted treatment differences.

Statistical Analysis
Basic documentation should include summary statistics for baseline and outcome data for each treatment group. Acceptance is contingent upon the product demonstrating a statistically significant difference when comparing study baseline to endpoint vs. that response for an appropriate control. Where appropriate, a non-parametric test will be used to assess safety evaluation data (normal vs. abnormal).