

## Acceptance Program Requirements



# Products for the Temporary Relief of Dry Mouth



## 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.

<b>Category:</b>	Products for the Temporary Relief of Dry Mouth
<b>Purpose:</b>	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.
<b>Scope:</b>	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.
<b>Notice Regarding Submission of Copyrighted Materials:</b>	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](mailto: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](mailto: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 Brand 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 Brand 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 clinical studies. If the product contains ingredients not on the generally recognized as safe (GRAS) list, at least one six-month clinical safety study may be required. See Appendix for details regarding clinical study protocols.
- iii. 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.
- iv. The product must have a pH between 5.5 – 10 demonstrated via laboratory testing.
- v. 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 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:

- Adamy, ST. Moisture retention in a (in vitro) porcine skin substrate. *Int J Cosmetic Science*, 2003. 25: p. 285-293
- Aframian, D.J., et al., Evaluation of a mucoadhesive lipid-based bioerodable tablet compared with Biotene mouthwash for dry mouth relief--a pilot study. *Quintessence Int*, 2010. 41(3): p. e36-42.
- Aykut-Yetkiner, A., A. Wiegand, and T. Attin, The effect of saliva substitutes on enamel erosion in vitro. *J Dent*, 2014. 42(6): p. 720-5.
- Barbe, A.G., et al., Efficacy of GUM(R) Hydral versus Biotene(R) Oralbalance mouthwashes plus gels on symptoms of medication-induced xerostomia: a randomized, double-blind, crossover study. *Clin Oral Investig*, 2017.
- Chevalier, M., et al., Antiseptic mouthwashes could worsen xerostomia in patients taking polypharmacy. *Acta Odontol Scand*, 2015. 73(4): p. 267-73.
- Constatin, M., et al. Skin hydration assessment through modern non-invasive bioengineering technologies. *Maedica J Clin Medicine*, 2014. 9(1): p. 33-38.
- Dost, F. and C.S. Farah, Stimulating the discussion on saliva substitutes: a clinical perspective. *Aust Dent J*, 2013. 58(1): p. 11-7.
- Epstein, J.B., et al., A double-blind crossover trial of Oral Balance gel and Biotene toothpaste versus placebo in patients with xerostomia following radiation therapy. *Oral Oncol*, 1999. 35(2): p. 132-7.
- Epstein, J.B., D.C. Villines, and H.Y. Sroussi, Patient reported outcomes of the -clinical use of a proprietary topical dry mouth product. *Spec Care Dentist*, 2015. 35(4): p. 197-204.
- Hitz Lindenmuller, I. and J.T. Lambrecht, Oral care. *Curr Probl Dermatol*, 2011. 40: p. 107-15.
- Kerr, A.R., et al., Comparison of two mouthrinses in relation to salivary flow and perceived dryness. *Oral Surg Oral Med Oral Pathol Oral Radiol*, 2015. 119(1): p. 59-64.
- Kirstila, V., et al., Effects of oral hygiene products containing lactoperoxidase, lysozyme, and lactoferrin on the composition of whole saliva and on subjective oral symptoms in patients with xerostomia. *Acta Odontol Scand*, 1996. 54(6): p. 391-7.
- Komulainen, K., et al., Oral health intervention among community-dwelling older people: a randomised 2-year intervention study. *Gerodontology*, 2015. 32(1): p. 62-72.
- Lajer, C., et al., Erosive potential of saliva stimulating tablets with and without fluoride in irradiated head and neck cancer patients. *Radiother Oncol*, 2009. 93(3): p. 534-8.
- Lopez-Jornet, M.P., et al., Clinical and antimicrobial evaluation of a mouthwash and toothpaste for xerostomia: a randomized, double-blind, crossover study. *J Dent*, 2011. 39(11): p. 757-63.
- Milleman, J.L., et al., Subjective Assessment of Enamelon(R) Preventive Treatment Gel in a Self-Reported Dry-Mouth Population. *Compend Contin Educ Dent*, 2016. 37(8): p. e5- 8.
- Morito, A., et al., Protective effects of polysaccharides and polyhydric alcohols in a dry mouth model in cultured cells. *Support Care Cancer*, 2012. 20(4): p. 725-31.
- Navarro Morante, A., et al., Natural products for the management of xerostomia: a randomized, double-blinded, placebo-controlled clinical trial. *J Oral Pathol Med*, 2017. 46(2): p. 154-160.
- O'Neill, I.D. and C. Scully, Biologics in oral medicine: Sjogren syndrome. *Oral Dis*, 2013. 19(2): p. 121-7.
- Oni, C., et al., Eligibility for clinical trials in primary Sjogren's syndrome: lessons from the UK Primary Sjogren's Syndrome Registry. *Rheumatology (Oxford)*, 2016. 55(3): p. 544- 52.
- Pedersen, A.M., et al., Oral findings in patients with primary Sjogren's syndrome and oral lichen planus--a preliminary study on the effects of bovine colostrum-containing oral hygiene products. *Clin Oral Investig*, 2002. 6(1): p. 11-20.
- Sato, K., et al., Effects of oral care in Down syndrome children with obstructive sleep apnea. *J Oral Sci*, 2010. 52(1): p. 145-7.
- Skrinjar, I., et al., Comparison between three different saliva substitutes in patients with

- hyposalivation. *Clin Oral Investig*, 2015. 19(3): p. 753-7.
- Soderling, E., et al., Betaine-containing toothpaste relieves subjective symptoms of dry mouth. *Acta Odontol Scand*, 1998. 56(2): p. 65-9.
  - Stewart, C.M., et al., Comparison between saliva stimulants and a saliva substitute in patients with xerostomia and hyposalivation. *Spec Care Dentist*, 1998. 18(4): p. 142-8.
  - Tenovuo, J., Clinical applications of antimicrobial host proteins lactoperoxidase, lysozyme and lactoferrin in xerostomia: efficacy and safety. *Oral Dis*, 2002. 8(1): p. 23-9.
  - Todorova P., et al. Biomimetic vs. traditional skin moisturization. *Cosmetics and toiletries*, 2015. 130 (8): p. 30-42.
  - Tschoppe, P., et al., Design of a randomized controlled double-blind crossover clinical trial to assess the effects of saliva substitutes on bovine enamel and dentin in situ. *BMC Oral Health*, 2011. 11: p. 13.
  - Warde, P., et al., A phase II study of Biotene in the treatment of postradiation xerostomia in patients with head and neck cancer. *Support Care Cancer*, 2000. 8(3): p. 203-8.
  - Wynn, R.L. and T.F. Meiller, Artificial saliva products and drugs to treat xerostomia. *Gen Dent*, 2000. 48(6): p. 630-6.
  - Yu, I.C., et al., Effects of mouthwash interventions on xerostomia and unstimulated whole saliva flow rate among hemodialysis patients: A randomized controlled study. *Int J Nurs Stud*, 2016. 63: p. 9-17.
  - ANSI/ADA Standard No. 116 – Oral Rinses 2020
  - ANSI/ADA Standard No. 116 – Oral Rinses 2020
  - ISO 16408:2015, Dentistry – Oral Care Products – Oral Rinses
  - ADA Brand Standards: [https://www.ada.org/-/media/project/ada-organization/ada/ada-org/files/resources/research/seal/ada\\_seal\\_brand\\_standards\\_nov2024.pdf](https://www.ada.org/-/media/project/ada-organization/ada/ada-org/files/resources/research/seal/ada_seal_brand_standards_nov2024.pdf)

## Appendix

### Clinical Protocol Guidelines for the Temporary Relief of Dry Mouth

The following guidelines are provided for the design and conduct of clinical studies to generate evidence for the evaluation of safety and efficacy of products intended to moisturize the mouth to relieve dry mouth symptoms. The term “dry mouth” includes xerostomia (subjective feeling of oral dryness) and hyposalivation (objective feeling of oral dryness). Dry mouth (xerostomia) may reflect reduced salivary flow, altered saliva composition, or mucosal dehydration, and symptoms do not always correlate directly with measured salivary flow. Clinical trials for the relief of dry mouth should clearly define the study criteria and must use validated patient-reported dry-mouth instruments or visual analog scales. Manufacturers are encouraged to submit their clinical protocols to the Council for review prior to the start of clinical studies. The information indicated below is applicable to each independent clinical study.

**Study design:** Clinical trials should be randomized whenever possible, with participants allocated to treatments through a randomization process. The trials can have a parallel or a crossover design. When using a crossover design, appropriate wash-out periods must be considered for the variables being tested. Studies should be blind regarding participants, examiners, and data analysis; when blinding is not possible, a justification must be provided. IRB approval is required for all studies involving human subjects. Each subject will have a complete oral cavity examination to determine eligibility for the study. 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. Studies must report all treatment groups, and an attempt should be made to assess the level of compliance of the subjects in the study.

**Number of studies:** At least two studies should be conducted at different sites and including a separate participant pool. Studies are expected to be independent, and free from direct control from the manufacturers. Studies are expected to adhere to the CONSORT or STROBE guidelines, as appropriate, and the checklist should be completed and uploaded with the submission. A minimum of thirty (30) day clinical studies are strongly suggested to show safety of the product.

**Sample size:** A sufficient number of subjects should be enrolled to ensure that appropriate statistical tests can be performed. The protocol should describe how sample size was determined, including all assumptions supporting the calculation and clearly defining the primary and secondary outcome variable(s) for which the study is being powered. A power of at least 80%, at an alpha error of 5%, is expected for variables leading to a Seal claim.

**Eligibility criteria:** Inclusion and exclusion criteria for participant's enrollment should be clearly described. 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. Subjects must be at least 18 years old and should be screened for potential participation in the study using a dry mouth inventory questionnaire to assess severity of reported dry mouth. Subject population 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 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. Subjects must refrain from the use of any non-study related product for symptom relief. Other criteria for inclusion/exclusion of subjects must be provided.

**Test product and comparator:** The test product should be compared with standard of care products/methods as defined by the ADA. Clear determination is to be made about the goal of the study to show superiority, equivalence or non-inferiority. Acceptance is contingent upon the product demonstrating a statistically significant reduction of dry mouth symptoms from baseline in comparison to that of an appropriate control.

**Clinical procedures:** The phases of the study (lead-in, test, wash-out, when applicable) should be clearly described, preferably using a diagram. The instructions given to participants regarding any study-specific procedures should be clearly described. The duration of the study, and when assessments will be performed, must be clearly described. For studies involving evaluators, their number and calibration methods should be provided, as well as intra/inter examiner agreement data.

**Assessments for efficacy:** Variables assessing efficacy should be clearly described and allow for a comparison between the test product and the comparators. Efficacy shall be demonstrated through subject response questionnaires administered at different time points throughout the length of the study as well as post-treatment using visual analog scale (VAS) or other subject response forms. Ensure that salivary testing, measuring salivary flow rates, is included for products claiming to increase salivary flow.

**Assessments for safety:** Variables assessing safety should be clearly described and allow for a comparison between the test product and the comparator. Evidence that the product does not adversely affect oral soft tissues, oral hard tissues, or on dental restorations (e.g. composite resins, porcelain, etc.) must be provided. Subjects should be examined in the course of the study for the presence of pathologic conditions such as oral ulceration, candidiasis, or other secondary infections of the oral mucosa. For products used in chronically or in immunocompromised populations, evidence should be provided that use does not increase risk of oral candidiasis, mucosal irritation, or microbial imbalance. Subjects should be questioned about difficulty swallowing, speech discomfort, or oral soreness. All adverse events should be reported including altered oral sensations for each observation period (e.g. burning mouth or altered taste). Information submitted for potential effects of agents 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.

**Statistical analysis:** Depending on the type of study (superiority, equivalence, non-inferiority), the statistical analysis plan should be described allowing for a comparison between the test product and the comparator, for all study variables, considering the predetermined power and significance level.

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