A Pilot Clinical Study to Assess Dry Mouth Relief After Using an Experimental Rinse Compared to a Negative Control

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The Procter & Gamble Company
Cincinnati, Ohio USA

A PILOT CLINICAL STUDY TO ASSESS DRY MOUTH RELIEF AFTER USING AN EXPERIMENTAL MOUTH RINSE COMPARED TO A NEGATIVE CONTROL

1 October 2019
Protocol Number 2019138

Signatures below indicate approval of the Protocol.

Sponsor:	The Procter & Gamble Company Worldwide Clinical Investigations—Oral 8700 Mason-Montgomery Road Mason, OH 45040

PII

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Clinical Scientist/Medical Monitor	PII
Clinical Trial Manager	
Statistician	
Clinical Data Manager	
Associate Director, Oral Care Clinical	

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LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation	Definition
AE(s)	Adverse Event(s)
AUC	Area Under the Curve
CFR	Code of Federal Regulations
CRF(s)	Case Report Form(s)
DMI	Dry Mouth Inventory
FDA	Food and Drug Administration
GCP	Good Clinical Practices
IRB/IEC	Institutional Review Board/Independent Ethics Committee
MD	Moisturization and Dryness
PPAQ I	Product Performance and Attributes Questionnaire I
PPAQ II	Product Performance and Attributes Questionnaire II
SOP(s)	Standard Operating Procedure(s)

PROTOCOL BODY

1. Study Objective

The objective of this pilot study is to determine if an experimental mouth rinse and a marketed dry mouth rinse are more effective in relieving dry mouth (as determined by the response to "relieving the discomfort of dry mouth" question from the modified Product Performance and Attributes Questionnaire I/ Moisturization and Dryness (PPAQ I/ MD)) compared to water.

2. Overall Study Design and Plan

This is a controlled, randomized, 3-treatment, 3-period crossover study in subjects with self-reported dry mouth symptoms as determined by subject responses to the Dry Mouth Inventory (DMI). A sufficient number of volunteers will be screened to ensure enrollment of up to 30 subjects at Acclimation. Subjects who meet the eligibility criteria will continue into the treatment phase of the study. Safety will be assessed by Oral examinations at Baseline/Day1 and Day 4. Subjects will complete questionnaires at Baseline (before product use Day 1 only), after immediate use, 30 minutes, 1 hour, 2 hours, and 4 hours after supervised product use on Day 1 and Day 4 of each period. The PPAQ II questionnaire will be completed in the morning of Day 4 of each period. Subjects will be randomly assigned to treatment sequences at the Baseline visit of Period 1. The treatment and washout periods will be repeated until all three treatment periods have been completed.

Table 1. Study Schedule by Procedure Type and Visit

Procedures	Screening/ Acclimation	Treatment Periods 1, 2, & 3					Washout
		Day 1 On site	Day 1 Off Site	Days 2 & 3 At Home	Day 4 On site	Day 4 Off Site	
Informed Consent	X						
Medical History	X						
Demographics	X						
DMI Questionnaire	X						
Inclusion/Exclusion	X						
Acclimation/Washout Product Distribution	X						
PPAQ II Questionnaire					X*		
Continuance Criteria		X			X		
Baseline MD Questionnaire		X					
Oral Examination		X			X		
Assigned Rinse / Water Product Distribution		X					
Supervised AM Product Use		X			X		
Immediate MD Questionnaire		X			X		
Product Usage Questionnaire		X**					
PPAQ I/ MD Questionnaire- 30 minutes		X			X		
PPAQ I/ MD Questionnaire- 1 hour			X			X	
PPAQ I/ MD Questionnaire- 2 hour			X			X	
PPAQ I/ MD Questionnaire- 4 hour			X			X	
4-hour Rating Questionnaire			X			X	

Product Diary		X	X	X	X		
Product Diary Return					X		
Treatment Product Return					X		
General Comments	X	X			X		
AEs		X			X		
Subject Accountability					X***		

* PPAQ II will be completed at home immediately after wake-up; **This questionnaire will be analyzed outside of this protocol
***P3-Day 4 only or when subject is dismissed from study.

Screening/Acclimation Visit

At the site, up to forty subjects will be asked to read and sign an informed consent form and will receive a signed copy for their records. Personal medical history information will be reviewed and retained as site source documentation. Demographic information will be recorded, and subjects will answer the DMI questionnaire to ensure study eligibility. Entrance criteria will be assessed. At total of thirty qualifying subjects will receive acclimation products and usage instructions. Subjects continuing will begin using these products in place of their normal oral hygiene products for the duration of the study. They will be instructed to brush their teeth in the morning of Day 1 visit. Subjects not meeting study entrance criteria will be dismissed.

Treatment Visits, Periods 1-3

Day 1 On-site Visit

Continuance criteria will be assessed. Subjects will complete a Baseline MD Questionnaire, followed by an oral examination. Subjects will then be randomly assigned to a treatment sequence (Period 1 only). Assigned treatment product kit boxes will be distributed, written instructions reviewed, and subjects will use the assigned products for the first time under supervision by site staff. A timer will be set for 4 hours and subjects will be instructed to refrain from eating, drinking, smoking, using their test products, using tobacco, using a medicated lozenge, chewing gum, or breath mints during the 4-hour time period. Immediately following product use, subjects will complete an Immediate MD Questionnaire and Product Usage Questionnaire (analyzed outside of this protocol). Subjects will remain on-site for the first 30 minutes to complete the PPAQ I/ MD 30-minute Questionnaire. Subjects will be instructed to complete PPAQ I/ MD at 1-hour, 2-hour and 4-hour and to fill out the 4-hour Rating Questionnaire at 4-hour. Subjects who received rinse products will be reminded to use them at least one more time (up to 5 times daily) after the last 4-hour questionnaire for Day 1 has been completed. Subjects will be reminded to bring their treatment boxes to their next study visit, and to refrain from using any rinse product the morning of their site visit.

Day 1 Off-site

Subjects will complete questionnaires, PPAQ I/ MD, at 1-hour (Day 1 PPAQ I/ MD 1h), 2-hour (Day 1 PPAQ I/ MD 2h), 4-hours (Day 1 PPAQ I/ MD 4h), and a 4-hour Day 1 Rating Questionnaire. Subjects will refrain from eating, drinking, smoking, using tobacco, using a medicated lozenge, chewing gum, or breath mints during the 4-hour time period until the last questionnaire for Day 1 has been completed.

All subjects will fill out a product diary tracking their product usage.

Days 2 and 3 At-home

Subjects will use the toothpaste products at home twice a day. Subjects that were assigned to the rinse products should use the rinse at least twice a day (no more than 5 times a day). All subjects will fill out a product diary tracking their product usage. Subjects will be reminded to follow the restrictions listed on the usage instructions. There is no eating or drinking restrictions for Day 2 and Day 3. Subjects from all groups will be allowed to sip unlimited amount of water.

Day 4 On-site Visit

Before coming to the site, subjects will complete a PPAQ II questionnaire (this questionnaire should be completed immediately after waking up). Subjects will also be sent a reminder to brush but not to use the assigned rinse product the morning, and to bring treatment products and the completed PPAQ II to their next site visit. Continuance criteria will be assessed, and take-home rinse products, product diaries and completed PPAQ II will be collected. An oral examination will be performed. After the oral exam, subjects will use the assigned products under supervision by site staff. A timer will be set for 4 hours. Subjects will remain on-site to complete the Immediate MD questionnaire and the 30-minute questionnaire (Day 4 PPAQ I/ MD 30 min). Subjects will be instructed to complete (Off-site) PPAQ I/ MD at 1-hour, 2-hour and 4-hour and to fill out the 4-hour Rating Questionnaire at 4-hour.

At this visit site staff will remind the subjects to refrain from eating, drinking, smoking, using any oral care products, using tobacco, using a medicated lozenge, chewing gum, or breath mints during the 4-hour time period. Subjects will be reminded to follow the restrictions listed on the usage instructions.

At Period 3 Day 4 washout product will be collected.

Day 4 Off-site

Subjects will complete a questionnaire, PPAQ I/ MD, at 1-hour (Day 4 PPAQ I/ MD 1h), 2-hours (Day 4 PPAQ I/ MD 2h), 4-hours (Day 4 PPAQ I/ MD 4h), and the 4-hour Day 4 Rating Questionnaire. After the Day 4, 4-hour questionnaires are completed, subjects will continue to use the study toothpaste for the wash-out period. Subjects will refrain from eating, drinking, smoking, using any oral care products, using tobacco, using a medicated lozenge, chewing gum, or breath mints during the 4-hour time period until the last questionnaire for Day 4 has been completed.

After the Period 3 Day 4 4-hour questionnaires have been completed, the subject will be dismissed from the study, and a Subject Accountability form will be completed.

Throughout the Study

General comments can be recorded at any time during the study. All Adverse Events (AEs) will be recorded. Any subject reported AE that remains unresolved by the end of the study should be followed up until resolution by the investigator/designee, and the resolution should be documented only as source documentation. If a subject is unreachable to determine whether the AE has been resolved, the attempts to contact the subject should be documented as source documentation. If, for any reason, a subject does not complete the study, an explanation will be entered on the Subject Accountability CRF. All data gathered on the subject prior to discontinuation will be made available to the Sponsor.

3. Inclusion Criteria

In order to be included in the study, each subject must:

- Provide written informed consent prior to participation and be given a signed copy of the informed consent form;
- Be at least 18 years of age;
- Be in good general health as determined by the Investigator/designee;
- Agree not to participate in any other oral care studies for the duration of this study;
- Agree to delay elective dentistry, including dental prophylaxis, until study completion, and to report any non-study dentistry received during the course of the study;
- Agree to refrain from the use of any non-study oral hygiene products for the study duration including mouth rinse and toothpaste (flossing is permitted if part of their normal routine);

- Self-report a dry mouth feeling according to the modified DMI questions. (Subject must answer at least 2 out of 4 questions with 'agree a little,' 'agree' or 'strongly agree');
- Agree to refrain from eating, drinking, smoking, using oral care products, using tobacco, using a medicated lozenge, chewing gum, or breath mints during the 4-hour test period;
- Agree to return for all scheduled visits and to follow all study procedures.

4. Exclusion Criteria

Subjects will be excluded from study participation where there is evidence of:

- Any condition or disease, as determined by the Investigator/Designee, that could be expected to interfere with examination procedures, with compliance, or with the subject's safe completion of the study;
- Severe periodontal disease, as characterized by purulent exudate, generalized mobility, and/or severe recession;
- Active treatment for periodontitis;
- Having a history of allergies or hypersensitivity to mouth rinse or ingredients in commercial dental products or cosmetics;
- Self-reported pregnancy or the intent to become pregnant during the study, or breast feeding;
- Full or partial dentures or any orthodontic appliances such as braces or aligners, or tongue or mouth piercing;
- Having diabetes;
- Inability to undergo any study procedure;
- Having untreated oral mucosal disease which in the opinion of the investigator could interfere with the study (e.g., current oral ulceration);
- Use of prescription systemic parasympathetic medications (e.g., Pilocarpine), for the treatment of the feeling of dry mouth;
- Currently under the care of a dental/medical professional specifically for the treatment of dry mouth (*at the discretion of the Investigator/Designee*);
- Self-reported mouth breathers (i.e., mouth breathing secondary to nasal obstruction);
- Evidence of gross intra-oral neglect or need for extensive dental therapy; or
- Currently undergoing radiotherapy and/or chemotherapy treatment.

5. Continuance Criteria

Subjects may be excluded from the study or the analysis if they:

- Have participated in any other oral care study since the last study visit;
- Since the last study visit, have developed any condition or disease or taken a new medication, which as determined by the Investigator/Designee could be expected to interfere with examination procedures, with compliance, or with the subject's safe completion of the study;
- Used any non-study oral hygiene products since the last study visit;
- Used study mouth rinse the morning of the study visit (*Day 4 only*); or
- Had any non-study dentistry, including dental prophylaxis performed since the last study visit.

6. Identity of Investigational Product(s)

- Acclimation/Washout: Burt's Bees Enamel Care Toothpaste (0.243% sodium fluoride, 0.13% w/v fluoride ion) and an Oral-B Indicator toothbrush
- Group 1: Burt's Bees Enamel Care Toothpaste (0.243% sodium fluoride, 0.13% w/v fluoride ion), Biotene Dry Mouth rinse (Purified Water, Glycerin, Xylitol, Sorbitol, Propylene Glycol, Poloxamer 407, Sodium Benzoate, Hydroxyethyl Cellulose, Methylparaben, Propylparaben, Flavor, Sodium Phosphate, Disodium Phosphate), and an Oral-B Indicator toothbrush
- Group 2: Burt's Bees Enamel Care Toothpaste (0.243% sodium fluoride, 0.13% w/v fluoride ion), Experimental mouth rinse (0.1% Sodium Hyaluronate), and an Oral-B Indicator toothbrush
- Group 3: Burt's Bees Enamel Care Toothpaste (0.243% sodium fluoride, 0.13% w/v fluoride ion), 15ml of water (on-site only) and an Oral-B Indicator toothbrush

7. Product Usage

At-home Toothpaste

Subjects will brush their teeth thoroughly, twice daily (morning and evening) as they normally do with the provided toothpaste and toothbrush. Subjects will be asked to use this toothpaste and toothbrush for the duration of the study, for both the acclimation/washout and treatment periods. Flossing and tongue brushing are permitted during the study if it is part of their normal routine.

Group 1 - Marketed rinse

On-site: Subjects will rinse their mouth with the assigned mouth rinse 15 ml for 30 seconds. Subjects will record usage in their product diaries. Subjects will not be allowed to use any mouth rinse during the 4-hour time period on Day 1 and Day 4.

At-home: Subjects will be instructed to use the rinse products at least twice a day and up to 5 times a day including any on-site usage, 15 ml for 30 seconds. Rinse can be used alone or after each time subjects brush. Subjects will record the usage in their product diaries.

Group 2 - Experimental mouth rinse

On-site: Subjects will rinse their mouth with the assigned mouth rinse 15 ml for 30 seconds. Subjects will record usage in their product diaries. Subjects will not be allowed to use any mouth rinse during the 4-hour time period on Day 1 and Day 4.

At-home: Subjects will be instructed to use the rinse products at least twice a day and to 5 times a day including any on-site usage, 15 ml for 30 seconds. Rinse can be used alone or after each time subjects brush. Subjects will record the usage in their product diaries.

Group 3 – Water/ No Rinse

On-site: Subjects will take, all at one time, a 15ml sip of water.

At-home: Subjects will continue brushing with provided washout toothpaste. Subjects will not be allowed to use any mouth rinse. Subjects will record their toothpaste usage in their product diaries.

8. Blinding, Labeling, and Shipping Plan

Acclimation/Washout take-home kit boxes will be labeled with study number, emergency phone number, distributor name/address, appropriate caution statements, content statement and other information as required by internal regulations and clinical SOPs. Treatment take-home kit boxes will be identically sized and labeled with a unique kit box number or code, study number, emergency phone number, distributor name/address, appropriate caution statements, content statement and other information as required by internal regulations and clinical SOPs. The shipping containers will be labeled with the clinical site address and a content statement listing study number and kit box numbers contained within. The site will be provided with a randomization treatment sequence and supplemental product.

The site will be provided with a code breaker report in a sealed envelope. The sealed code breaker report contains documents that list the kit box number or treatment code while the identity of the treatment products is hidden by an opaque scratch-off seal. If the study blind needs to be broken, an individual subject's investigational product may be ascertained by opening the sealed code breaker report, locating the subject's kit box number or treatment code and scratching off the opaque seal to reveal the treatment identity. The sealed code breaker report will be opened if a clinically serious AE occurs or management of the subject requires knowledge of the identity of the investigational product. The Investigator should immediately inform the Sponsor that the code will be broken and record the date, time and reason for breaking the code in writing. After the study is complete and the study database has been finalized and locked, the site will return the code breaker report to the Sponsor using the self-addressed, stamped envelope provided by the Sponsor.

9. Method of Assigning Subjects to Treatment Groups

Study Design	N	# of Treatments	# of Periods	Treatment Sequences	Number of Subjects Per Sequence
Crossover	30	3	3	ABC, ACB, BAC, BCA, CAB, CBA	5-6

Treatment Sequence Schedule

Each of the eligible subjects will be randomly assigned to one of the treatment sequences. Subjects will be assigned to a treatment sequence in the order they come to the site during their first Baseline visit using a Treatment Sequence Schedule. The site will keep the Treatment Sequence Schedule while the study is on-going. Should a subject miss a treatment period, that treatment in the sequence will be skipped.

10. Determination of Sample Size

Sample size is based on logistical considerations.

11. Safety Variables

Oral Examination

Assessment of the oral soft tissue is conducted via a visual examination of the oral cavity and perioral area utilizing a standard dental light, dental mirror, and gauze. The structures examined include the gingiva (free and attached), hard and soft palate, oropharynx/uvula, buccal mucosa, tongue, floor of the mouth, labial mucosa, mucobuccal/mucolabial folds, lips, and perioral area.

Assessment of the oral hard tissues are conducted via a visual examination of the dentition and restorations utilizing a standard dental light, dental mirror, and air syringe. All abnormal findings are recorded and categorized by their location with hard tissue findings categorized as “other-oral.” An AE is recorded if a new abnormal finding is noted after treatment application or any abnormal finding noted prior to treatment application increases in severity after treatment is applied.

12. Hypotheses

The following hypotheses will be tested for each response to the PPAQ I/ MD questions, the PPAQ II questions, and the rating questions at each applicable time point:

Null: The mean response is equal between the Experimental rinse and Water.

Alternative: The mean response is not equal between the Experimental rinse and Water.

Null: The mean response is equal between the Marketed rinse and Water.

Alternative: The mean response is not equal between the Marketed rinse and Water.

The primary endpoint will be the response to “relieving the discomfort of dry mouth” from the modified PPAQ I/ MD two hours after supervised product use on Day 4 of treatment. Responses to all other questions and time points will be of secondary interest.

13. Statistical and Analytical Plans

Responses to the questions will be analyzed separately using a general linear mixed model for a crossover with period and treatment as fixed effects and subject as a random effect. Carryover will be assessed and if reasonably appropriate, it may be included in the statistical model. Statistical comparisons will be two-sided with a significance level of 0.10. No adjustments will be made for multiple comparisons. Additional analyses of the data may be performed. This may include but is not limited to area under the curve (AUC).

APPENDIX I

Advertising

If the Oral Health Science Center chooses to advertise for subjects, whether in professional or consumer publications, radio, television, or any other means, all advertising must be approved by the IRB prior to use, documented, and retained.

Confidentiality

Subject files will be maintained in a locked location for the duration of the study. The recipients will treat this information confidentially. In the event of any publication regarding this study, subject identity will not be disclosed.

Direct access to study records and source data/documentation, including subject medical records, will be provided as needed to appropriate parties for the purpose of trial-related monitoring, auditing, IRB/IEC review, and regulatory inspection. Prior to participating in the study, subjects will consent, in writing, to the release of their medical records for said purposes.

Data Collection

The Data Manager will supply the paper and/or electronic CRFs to be used in this study. It is the responsibility of the Investigator to maintain and submit accurate and timely CRFs to the Sponsor. All hard copy CRFs will be filled out legibly in ink.

All questions should be answered. For paper CRFs, if an entry requires correction, a single line will be placed through the entry so as not to obscure the original record, the corrected entry will be initialed and dated by the individual making the change, and a reason will be given for the change. There will be no whiteouts or erasures. For electronic CRFs, if an entry requires correction, the change is made directly to the CRF in the database, the user is prompted to provide a reason for the change, and the correction is logged in by an electronic audit trail.

As necessary, the Data Manager may make specified allowable changes to the database without issuing a query to the site, as agreed upon by study site per this protocol. Examples of allowable changes include incorrect date formats, incorrect current year recorded (as in the start of a new year), and unambiguous spelling errors. Changes to common abbreviations and symbols to equivalent text to meet system or coding constraints (e.g., @ = at, ~ = approximately), may also be allowable. Values that are ambiguous or open to interpretation will be queried to the sites. It is the responsibility of the Data Manager to ensure all changes are supported by information contained elsewhere and/or are unambiguous.

Source Documents

The Investigator has the responsibility for ensuring that all source documents (i.e., study and/or medical records) and CRFs are completed and maintained according to the study protocol and are available at the site. Any CRF used as a source document must be identified as such in the Investigator Notebook.

Good Clinical Practices

This study is conducted in compliance with applicable sections of the US Federal Regulations governing informed consent (21 CFR 50), IRBs (21 CFR 56), study conduct (21 CFR 312) and

the International Conference on Harmonization's Good Clinical Practice Consolidated Guidelines, [ICH-GCPs, as published by the FDA on 9 May 1997, Federal Register, Volume 62, Number 90 pages 25691-25709]). During the course of the trial, the clinical site is monitored by P&G staff (Clinical Trial Manager or designee) to ensure compliance with the Protocol, regulations and guidelines, adequacy of the equipment and facilities, and satisfactory data collection.

Informed Consent

A subject consent form will comply with all applicable regulations governing the protection of human subjects. The elements of informed consent and the documentation of informed consent are specified in 21 CFR 50.25 and 50.27 and/or ICH GCPs chapter 4. Each subject must sign and date an informed consent to serve as a participant in the study. A signed copy of the consent form will be given to the subject and a signed copy will be retained by the Oral Health Science Center. Subjects may withdraw from participation in the study at any time. Additionally, the Investigator may withdraw subjects from the study if it is in the best interest of the subjects. The reason for all subject withdrawals from the study will be documented on the appropriate CRF.

Institutional Review

Prior to study initiation, the Investigator must obtain institutional review and approval of both the Protocol and the consent form, in compliance with the US Code of Federal Regulations, Title 21, Part 56 or the ICH-GCPs Consolidated Guidelines, Chapter 3. The Investigator maintains any original authorization letter(s) and forwards copies to P&G. IRB approval letters should include the study title, P&G study number, the address of the IRB, date of request, and the signature of the IRB chairperson/designate. Additionally, the letter must acknowledge that both the Protocol and consent form have been approved by the IRB, with notification of any changes required. The study does not begin until P&G has received written confirmation of IRB approval. This IRB shall also review the investigation at least once a year during study execution. The Investigator notifies the IRB when the study is terminated.

Monitoring

Prior to commencement of the study, an initiation meeting will be held with the appropriate Oral Health Science Center personnel to review the objectives and procedures of the clinical trial. To assure accurate, complete, consistent, and reliable data, the Oral Health Science Center and study procedures will be monitored by a Clinical Trial Manager in accordance with 21 CFR 312 and ICH GCPs Chapter 5.

The Oral Health Science Center study coordinator is expected to contact the Clinical Trial Manager or designee as needed regarding study concerns and/or questions.

Protocol Amendments/Changes

Changes to the Protocol following Institutional Review Board (IRB) approval affecting the safety of subjects, scope/objectives of the investigation, or the scientific quality of the study are documented as amendments. Such changes require P&G, Investigator, and IRB approval prior to implementation, unless immediate action is required to safeguard subject safety. Administrative/minor changes (e.g., typos, changes in P&G personnel [excluding medical monitor], etc.) are documented as revisions but do not have to be submitted as amendments unless required by the IRB. Any change in P&G's monitoring staff, Clinical Trial Manager or Medical Monitor during the conduct of the study, must be reported to the Investigator.

Serious Adverse Event Reporting

A *serious adverse event* is defined as an event, which suggests a definite hazard or handicap to the subjects. Serious adverse events are any events resulting in death, life threatening situation, disability or permanent damage, hospitalization or prolongation of existing hospitalization, or congenital anomaly/birth defects; events requiring intervention to prevent permanent impairment/damage; or other serious (important) medical events.

When an Investigator is notified of a serious AE, the Investigator must promptly (within 24 hours) notify the Sponsor (Clinical Trial Manager or the Medical Monitor) of the serious or unexpected event, regardless of causality. Within 5 working days, a written and/or electronic report describing the circumstances of the event must be submitted to the Sponsor. The Investigator will be responsible for SAE reporting to the IRB.

Study Medication Dispensing, Storage and Accounting

Study products are stored in a secure area, under environmental condition as required by label instructions or as described in the Protocol, and dispensed only under the authorization of the Investigator. The storage condition shall be properly documented. Both the receipt and dispensation of all test products (used and unused) are documented using forms provided by P&G or suitable forms provided by the site. Study products are returned to P&G following the trial, or alternatively, they are destroyed at the clinical site provided the site has an existing SOP for the destruction of clinical materials and prior written approval from P&G.

Study Termination

The study is terminated upon completion of all subject treatments and evaluation. The study may be discontinued at any time.

Subject Consent

The Investigator obtains written informed consent for each subject prior to that subject's participation in the study, per the US Code of Federal Regulations, Title 21, Parts 50.25 and 50.27 and ICH-GCPs, Chapter 4, subpart 4.8. Subjects, or their legal guardian, are required to read, sign and date an IRB approved consent form with the Investigator also maintaining a signed and dated copy. The subject or legal guardian will be given a copy of the consent form. All study procedures must be explained in non-technical terms.

APPENDIX II

Listing of Questionnaires

DMI Questionnaire

Subjects must answer 2 or more of the 4 questions positively in order to continue into the study.

How much do you agree or disagree that you experience the following? (strongly disagree, disagree, disagree a little, agree a little, agree, strongly agree)

1) No moisture in the mouth
2) Lips sticking to teeth
3) Tongue sticking to roof of mouth
4) Throat feels dry

Baseline MD Questionnaire

Subjects to answer:

1) How moist does your mouth feel now? (0=not at all to 10= very moist)
2) How dry does your mouth feel now? (0=very dry to 10=not dry at all)

Immediate MD Questionnaire

Subjects must answer:

1) How moist does your mouth feel now? (0=not at all to 10= very moist)
2) How dry does your mouth feel now? (0=very dry to 10=not dry at all)

Product Use Questionnaire

Considering everything about the mouthwash product you used today, please indicate the one word or phrase which best describes your overall opinion of this product. (Select one response)- excellent=5, very good=4, good=3, fair=2, poor=1

What are all the things you **LIKED** about the mouthwash product you used today? Please be specific. Free-form text

What are all the things you **DID NOT** like about the mouthwash product you used today? Please be specific. Free-form text

Considering your experience **while using** the mouthwash product you used today, how would you rate the mouthwash for each of the following characteristics? (Select one response for each attribute) excellent=5, very good=4, good=3, fair=2, poor=1:

1) Overall taste
2) Overall sweetness

3) Level of thickness to coat mouth tissue
4) Flavor strength
5) Soothes while I swish

Considering your experience **immediately after** using the mouthwash you used today, how would you rate the mouthwash for each of the following characteristics? (Select one response for each attribute- excellent=5, very good=4, good=3, fair=2, poor=1):

1) Leaves a cooling sensation in mouth
2) Freshens my breath
3) Leaves my whole mouth feeling protected
4) Leaves a pleasant taste in my mouth

Which of the following descriptors apply to the sample you just evaluated? (Circle all that apply): Metallic, Medicinal, Thick, Burn, Tingle, Moisturizing, Chalky, Filmy, Sweet, Watery, Mild, Bitter, Sour, Soothing, Sharp, Fruity, Minty, Refreshing, Cooling, Slimy, Clean, Astringent, Harsh, Numbing, Dry, Bland, Oily, Smooth

PPAQ I/ MD Questionnaire

Since you have been used the product, please rate each of the following at this timepoint: (Select one response for each attribute)- excellent=5, very good=4, good=3, fair=2, poor=1:

1) Relieves the discomfort of your dry mouth
2) Feels comfortable in your mouth
3) Soothes your mouth
4) Allows you to speak without difficulty
5) Effectively moistens your mouth
6) Effectively lubricates your mouth
7) Helps to freshen your breath
8) Protects your mouth from drying out
9) Provides whole mouth comfort
10) Helps you to swallow without difficulty
11) Helps your mouth feel “normal”

Subjects must answer:

1) How moist does your mouth feel now? (0=not at all to 10= very moist)
2) How dry does your mouth feel now? (0=very dry to 10=not dry at all)

PPAQ II Questionnaire

Since you have been using the product over the last 4 days, please rate each of the following as they apply to the rinse study product: (Select one response for each attribute)- excellent=5, very good=4, good=3, fair=2, poor=1:

1) Provides relief all night
2) Reduces the number of times you wake up from dry mouth
3) Feeling less parched when you wake up
4) Having a long-lasting dry mouth relief

5) Having a long-lasting lubricating effect
6) Having a long-lasting moisturizing effect

4-hour Rating Questionnaire

1) How would you rate the overall moisturization of your mouth after using the product? 0= does not provide moisturization at all to 10=best possible moisturization
2) How would you rate the long-lasting moisturization effect of the product? 0= does not provide long lasting moisturization at all to 10=best possible long lasting moisturization
3) How would you rate the overall relief of your dry mouth after using the product? 0= does not provide relief at all to 10=best possible relief
4) How would you rate the long-lasting dry mouth relief of the product? 0= does not provide long lasting relief at all to 10=best possible long-lasting relief