Title: Effect of Curved Design Soft-Picks® on Plaque Accumulation on Patients with Signs of Gingivitis

Project Code: Curved Pick Study (CPS)

Version#:6

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STUDY OVERVIEW

Study Title (ID)	Effect of Curved Design Soft-Picks® on Plaque Accumulation on Patients with Signs of Gingivitis
Project	The aim of this study is to evaluate the efficacy of a new interdental cleaning device called Soft-Picks® Advanced, as compared to a leading brand floss; and, how ease of use can promote the establishment of a hygienic routine of cleaning interproximal spaces. The Soft-Picks® Advanced has a new design allowing a user to easily access to difficult interdental sites, such as spaces between premolars and molars. As compared to conventional Soft-Picks®, it has a unique handle design with an increase in thickness. This study is a single center with parallel design, single blinded, which will randomize eligible subjects into two treatment groups.
Subjects	It is planned that 53 subjects will be enrolled and randomized with 15% dropout, in order to complete with a minimum of 44 subjects (22 subjects per treatment group) which is eligible for statistical analysis. *Subjects must:* • be age 18 -70 years • be routine manual toothbrush users • have no or little[1] experience with interproximal cleaning devices, such as floss or interdental brush • have signs and symptoms of gingivitis, defined by: all PD ≤4mm and BOP ≥10% but ≤50% of sites. *Subjects must **not**:* • have participated in an oral care study in the previous 90 days *Subjects may **not**:* • have any tooth site with ≥5mm PD or ≥3mm attachment loss [1] Definition of little: no habitual use of any interproximal cleaning devices; subjects cannot recall the last time he/she used it, and/or he/she can recall such experience only at a dental office visit
Study Design	• Single Center • Parallel design • Randomized: 2 treatment groups (1 Device-A Group and 1 Device-B Group) with 53 randomized to complete with minimum of 44 subjects (22 subjects per Treatment Group) balanced for gender • Home use period of total 28 days (4 weeks) • Single Blinded (efficacy examiner(s))
Treatment Groups	• Device-A: Oral-B Glide Pro-Health Floss Original • Device-B: Sunstar GUM Soft-Picks® Advanced

Clinical Evaluations	• Oral Examination • Lobene - Turesky Modification of the Quigley-Hein Plaque Index (2) • UNC Modified Gingival Index (UNC-GI) • BOP - bleeding on probing • PPD - probing pocket depth • CEJ - cementoenamel junction • Safety (2) Turesky S, Gilmore N, Glickman I. Reduced plaque formation by the chloromethyl analogue of Vitamin C. J Periodontol 1970; 41: 41-43.
Subject Visit Summary	**Visit 1 – Screening and enrollment:** Informed Consent; Screening Medical/Dental History and Demographics; Screening Oral Exam; Screening Clinical Indices: MQH-PI (designated teeth only), UNC-GI (full mouth); PPD, CEJ and BOP (full mouth); Teeth Site Selection(s); Enrollment, Prophylaxis; Regime Product Dispense: Assigned Manual Toothbrush and Dentifrice; Supervise Use; Follow-up Visits Scheduled **Visit 2 – Baseline:** 12-18 hours of Plaque Accumulation, and 3-6 hours of Diet Restriction Observed; Randomization; AE Monitoring: Interview and Oral Exam; Taking Clinical Indices: MQH-PI, UNC-GI (designated interproximal sites); PPD, CEJ and BOP (designated interproximal sites) Dispense: Assigned Products; Usage Instruction, Supervise Use; Distribute Subject Diary; Follow-up Visits Scheduled **Visit 3 – Two (2) weeks observation:** 12-18 hours of Plaque Accumulation and 3-6 hours of Diet Restriction Observed; Compliance Monitoring; AE Monitoring: Interview and Oral Exam; Taking Clinical Indices: MQH-PI, UNC-GI (designated interproximal sites); Follow-up Visits Scheduled **Visit 4 – Four (4) weeks observation:** 12-18 hours of Plaque Accumulation and 3-6 hours of Diet Restriction Observed; Compliance Monitoring; AE Monitoring: Interview and Oral Exam; Taking Clinical Indices: MQH-PI, UNC-GI (designated interproximal sites); PPD, CEJ and BOP (full mouth); Prophylaxis and Referral for Further Care, if indicated; Product & Diary Return; Subject Compensation, Questionnaire and Study Dismissal

Home Use:	• Daily afternoon/evening use of assigned treatment products until return for final visit • Record product performance and experience on a diary • All studied treatment products are to be used with: 1) Crest Cool Mint Gel toothpaste and 2) Oral-B Indicator manual toothbrush • No other oral hygiene aids allowed during the study

List of Abbreviations

Abbreviation	Definition
ADA	American Dental Association
AE	Adverse Event
ANOVA	Analysis of Variance
B	Buccal
BOP	Bleeding on Probing
CAL	Clinical Attachment Level
CFR	Code of Federal Regulation
CRF	Case Report Form
CRO	Contract Research Organization
DDE	Direct Data Entry
DF	Distofacial
DL	Distolingual
EC	Ethics Committee
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
GBI	Gingival Bleeding Index
GCP	Good Clinical Practice
GM	Gingival Margin
ICH	International Conference on Harmonization
IP	Interproximal
IRB	Institutional Review Board
ITT	Intent to Treat
IU	Interproximal Unit
L	Lingual
LL	Lower Left
LR	Lower Right
MF	Mesiofacial
UNC-GI	UNC (modified) Gingival Index
ML	Mesiolingual
MTB	Manual Toothbrush
MQH-PI	Lobene - Turesky Modification of the Quigley-Hein Plaque Index
PPD	Probing Pocket Depth
QTS	Quadrant Tooth Site
SAE	Serious Adverse Event
SAS	Statistical Analysis Software
UADE	Unanticipated Adverse Device Effect
UL	Upper Left
UR	Upper Right

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Background

Introduction & Product Description

Product Description:

In order to maintain good gingival and periodontal health, the most effective approach is to regularly remove bacterial biofilm, which poses threats to develop gingivitis and likely periodontitis, if unremoved. The biofilm is removed by toothbrushing, a most known method; however there is still a risk of developing periodontal diseases when they are left unremoved, especially in interproximal spaces. Interproximal spaces are naturally difficult to reach for plaque removal. The teeth contours are different among people; therefore there has been need of interproximal cleaning devices, such as floss and interdental brushes. Along with such product development, there have been many clinical studies which succeeded in showing that the combination of using a toothbrush and interproximal cleaning devices improve the reduction in biofilm accumulation. This practice is recommended by the American Dental Association (ADA)[3]:

> The ADA recommends brushing twice a day and cleaning between teeth with floss (or another interdental cleaner) once a day.

According to the American Academy of Periodontology (AAP) survey[4], 27% of US adults have admitted they have provided false information regarding their flossing routine to their dentists. In addition, the survey shows that 36% of Americans would rather do an unpleasant activity, such as cleaning the toilet, rather than flossing. This indicates that establishing a routine to floss regularly is difficult and challenging, yet it has been recommended that with regular brushing, interproximal cleaning is an important aspect to maintain good gingival and periodontal health.

In order to overcome such patient compliance problem, different types of interproximal cleaning devices have been developed and released in the market. Since their release, interdental brushes have gained popularity because they are easy to use. Soft-Picks® by Sunstar G·U·M is one of the many types of interdental cleaning devices in the market; however, it has a unique design that is different from other devices. It has an advantageous design which uses gentle rubber bristles (small ridges), as compared to regular nylon bristles, which can potentially cause gingival irritation and trauma.

The aim of this study is to evaluate the efficacy of a new interdental device called Soft-Picks® Advanced, as compared to a leading brand floss, and how ease of use can promote the establishment of a hygienic routine of cleaning interproximal spaces. The Soft-Picks® Advanced has a new design allowing a user to easily access difficult interdental spaces, such as spaces between premolars and molars. As compared to conventional Soft-Picks®, it has a unique handle design with an increase in thickness and curvature.

[3] http://www.ada.org/en/science-research/ada-seal-of-acceptance/product-category-information/floss-and-other-interdental-cleaners
[4] https://www.perio.org/consumer/quarter-of-adults-dishonest-with-dentists

Risks and Benefits
Participants enrolled in this study may experience risks associated with standard dental examinations, dental prophylaxis, tooth brushing and use of manual interdental oral hygiene devices. Risks are not limited to but may include the following:

- Gingival inflammation, irritation, bleeding or abrasion from tooth brushing and/or use of the investigational (interdental) devices.
- Minor pain, discomfort and bleeding may be present during periodontal probing.
- Gingival and/or tooth pain or sensitivity, loosened or damaged dental restorations may occur as a result dental prophylaxis
- Jaw soreness may occur as a result of opening the mouth for examinations and procedures.

Justification of Treatment Periods and Regimens

Visit 1: Screening and enrollment
Study participants are consented and selected based on a standard set of eligibility criteria in order to limit exposure to subjects who may experience undue risk by participating, and to select a panel exhibiting moderate levels of plaque accumulation and mild level of gingival inflammation, in whom a response may be evaluated over time.

Visit 2: Baseline
This is a baseline assessment following 21 days from the screening and enrollment visit. The randomization and assignment of home use treatment regimen are defined.

Visit 3: Two (2) weeks follow-up
This is the first efficacy assessment following 14 days of the assigned home use regimen, as well as the mid-point safety visit. It was selected as a point in time deemed sufficient to elicit responses in both the clinical and sub-clinical manifestations of change in oral health status, should any changes occur.

Visit 4: Four (4) weeks follow-up
This is the secondary efficacy assessment following 28 days of the assigned home use regimen, as well as the final safety visit. It was selected as a point in time deemed sufficient to elicit responses in both the clinical and sub-clinical manifestations of change in oral health status, should any changes occur.

Subject Population to be Studied
This study shall be conducted with male and female volunteers in good general health, aged 18 -70 years who have signs and symptoms of gingivitis. Complete inclusion/exclusion criteria are provided in Section 4.0.

Statement of Compliance
This study is being conducted according to the ICH Guideline for Good Clinical Practices (GCPs). All study materials are to be reviewed by the UNC Institutional Review Board (IRB) prior to enrollment of any subject or dispense of any test article. The ethical

principles for the treatment of human subjects on this study have their origin in the Declaration of Helsinki.

All study personnel will be required to have completed Human Subjects Protection Training and Good Clinical Practice Training. A copy of each person's completion certificate is maintained in the GO Health Center and will be added to the Study Master File. All study staff will receive training on all aspects of the protocol. Study personnel will ensure that the research study is conducted, recorded and reported in accordance with the protocol, Standard Operating Procedures (SOPs), Good Clinical Practice (GCP) and the applicable regulatory requirements. The study coordinator will monitor source documentation daily to ensure that data fields are complete and accurately reflect study activities.

Study Objective(s)

Primary Objective
The primary objective of this study is to evaluate the possible difference in interproximal plaque accumulation between lead-brand floss users and Soft-Picks® Advanced (non-wired interdental brush) users

Secondary Objective(s)
The secondary objectives focus on the relationship between a user and a product. This is important due to the fact that periodontal preventative care is mostly accomplished by a public health approach; therefore the secondary objectives of the study are:

- to evaluate the user experience in terms of ease of product use and motivational level to use (level of difficulty in hygienic routine establishment);
- to evaluate the level of correspondence between user experience and product performance (satisfaction level).

Also the secondary objective of the study contains evaluation of the possible difference in gingival inflammation between lead-brand floss users and Soft-Picks® Advanced (non-wired interdental brush) users

Study Design

Primary Endpoint
The primary endpoint is the reduction from baseline in interproximal plaque accumulation as measured by MQH-PI following a period of home use for 14 and 28 days.

Secondary Endpoint(s)
The Secondary Endpoints of the study are:

- performance of an assigned product based on user experience;
- reductions from baseline in gingivitis as measured by interproximal UNC-GI, PPD and BOP post home use for 28 days;
- safety of the study products;

Trial Design
This is randomized, parallel, single-blinded study design. This is a standard study design used to compare treatments following a period of home use of the assigned study products.

A summary of activities and evaluations at each study visit is outlined in Section 5.0.

Controls to Minimize Bias
In order to minimize bias, all study participants will be randomly allocated to a treatment assignment. Additionally, applicable staff member(s) who are performing efficacy assessments will be blinded to the treatment assignment of the study subjects.

Randomization of Subjects
Subjects shall be allocated to the treatment groups according to a pre-defined randomization schedule. Randomization will be blocked by sex only.

Blinding
The blinded staff member(s), e.g., Examiners, shall be blinded to the treatment allocation of the study subjects at the time of randomization and efficacy evaluation period. All other personnel involved with the conduct of this study will not be blinded. If the Principal Investigator is also working in a capacity that requires that he/she directly assess an efficacy endpoint, he/she shall be blinded until all efficacy endpoint evaluations are completed.

Product allocation shall be reported in a database so that compliance and randomization can be monitored for accuracy. However, the blinded staff member(s) shall not have access to the database until all efficacy evaluations are completed.

Study Regimen and Product Labeling

Study Regimens
The study regimens consist of the following:

- **Regimen 1/Interproximal Cleaning Aids**
  Once daily use of GUM Soft-Picks® Advanced or Oral-B Glide Pro-Health Original each afternoon or evening at approximately the same time every day

- **Regimen 2/Manual Toothbrush**
  Twice daily use of: Oral-B Indicator manual toothbrush & Crest Cool Mint Gel dentifrice.

Product Labeling

Products, Treatments and Medications not Permitted on Study
Once a subject is enrolled on-study, the use of any additional oral hygiene treatments and aids other than those prescribed is prohibited. A list of prohibited devices and aids

includes but is not limited to: power toothbrushes, other types of interproximal cleaning aids, mouthwash, chewing gum, oral irrigators or whitening products. The use of any dentifrice other than Crest Cool Mint Gel is also prohibited.

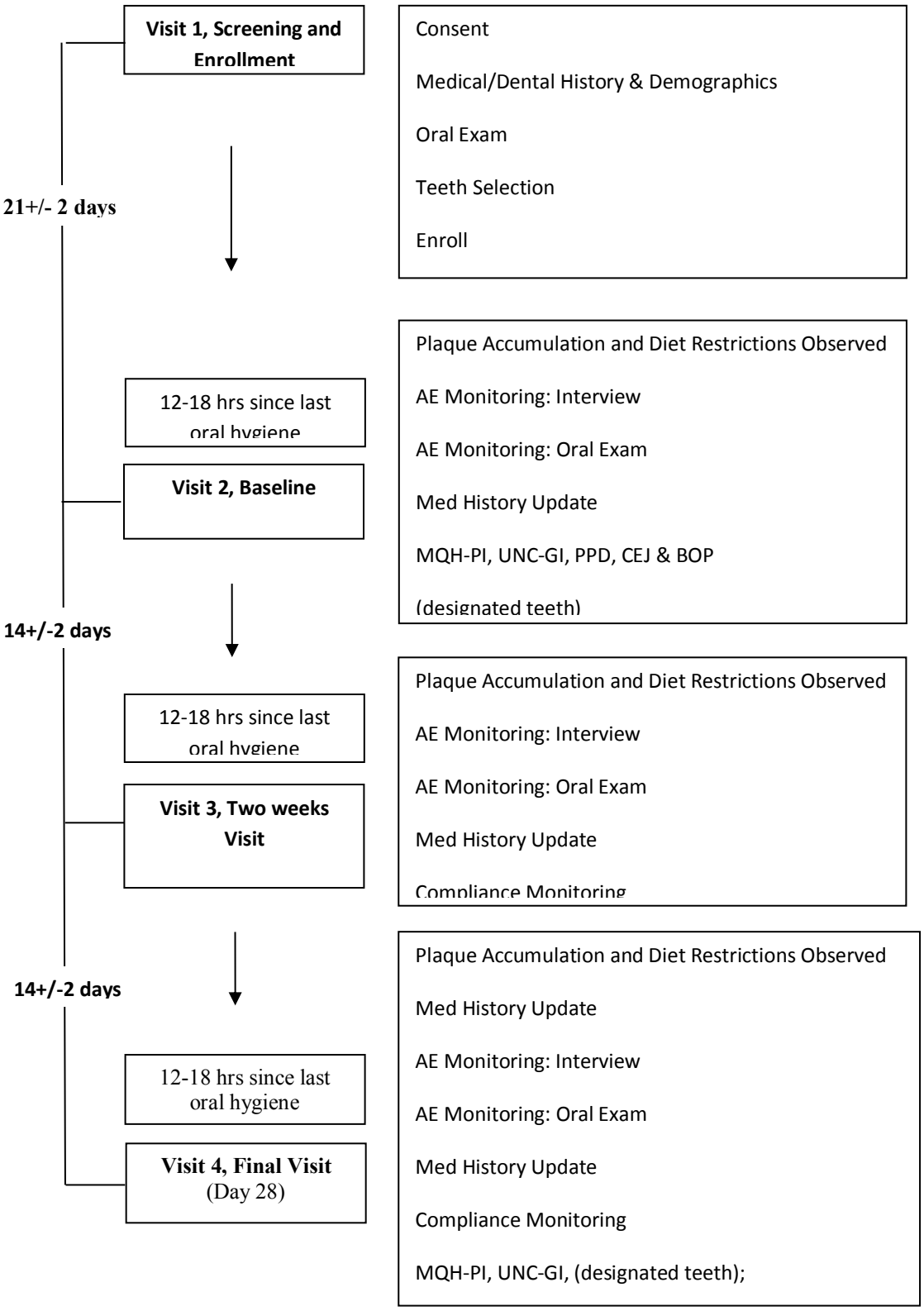
The use of antibiotics or antibacterial agents is prohibited. Chronic use (i.e., two weeks or more) of any medication known to affect periodontal status (e.g., phenytoin, calcium antagonists, cyclosporine, non-steroidal anti-inflammatories and anticoagulants) is also prohibited. (Daily use of 81mg Aspirin is allowed).

All deviations shall be documented. Participants who have used prohibited products, devices and/or medications may be discontinued. Upon discovery of such usage, the Principle Investigator shall be notified for discussion and reassessment of eligibility and study continuation.

In the event that an enrolled subject requires dental care outside the scope of the study, he/she may be discontinued from the trial and no further procedures performed, other than safety assessments (e.g., oral exam and adverse event interview).

Study Sequence Diagram

Schema 1 below illustrates the sequence of examinations and treatment periods for study subjects.



Expected Duration of Study
Study participation period per individual is approximately 49 days.

Discontinuation Criteria/Stopping Rules
Individual participants may be removed from the study if significant non-compliance is noted. Additionally, if in the opinion of the investigator, the health or safety of a subject is affected adversely by participation in the study, the subject shall be removed. A subject may be replaced in the event of withdrawal or dropout.

Maintenance of Randomization Information

Sponsor

Once study procedures have been completed, a copy of the completed randomization list shall be collected from the site for the Sponsor files. Once the study is completed and all data cleaned, the randomization schedules will be merged with the overall database for analysis.

Site
A randomization list will be created by UNC Dental Data Manager and provided only to the assigned personnel in the GO Health Center who are responsible for randomization and product dispensation. The randomization ID and the corresponding treatment shall be transcribed into the study case report forms (CRFs). It is the responsibility of the designated Site personnel to maintain the integrity and the blind of randomization. The original completed list shall remain in the site master file and be available for review by study Monitor(s) to ensure compliance.

Procedures for Breaking Randomization Codes
Emergency unblinding for adverse events may be performed by requesting the participant's specific treatment assignment from the Site personnel delegated randomization responsibilities. Such an event should be documented and include the number of the subjects unblinded, the date, and a list of all 'blinded' personnel that received the unblinded information. If a subject's treatment assignment is unblinded, the sponsor and the IRB must be notified immediately by telephone or e-mail.

Study Data: Source Documentation, EDC Reporting and Data Quality Control

Source Documentation
Source data includes all information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical investigation used for reconstructing and evaluating the investigation. This information may be collected prior to (e.g., medical history), during or after the trial.

Good documentation practices shall be followed to ensure that study results are built on a foundation of credible and valid data. Also, to ensure an independent evaluator may reconstruct the trial as it happens.

Source data may be captured as follows:

- on paper or in electronic site study records or other health facility records for later transcription into eCRFs, or
- directly reported into the eCRFs at the time of study observation or procedure completion (direct data entry (DDE))

A combination of the above is typical and expected for this study. Source data shall be captured as follows:

Site or other Health Facility Records (paper)*	**Directly in the eCRFs**
Consent process & disposition	Clinical Indices (e.g., plaque index)
Pre-existing Medical/Dental History & Updates	Oral Examinations
Subject Diary Metrics	Demographic Information
Product dispense and return	Vitals
Safety and Eligibility	Height & Weight
Adverse Events & Deviations	Tooth Status

***Note:** Site study documents (paper) shall also be used when DDE is not possible (e.g., lost internet connection).

Source documents to capture original data for later transcription shall have adequate Site/facility and subject identifiers, dates, etc., as appropriate and must be legible.

Key Reminders:

- Any source data captured directly in the eCRFs shall occur at the time of observation or procedure completion
- All transcribed data must have paper/electronic source documents for verification
- If handwritten, a black pen should be used to capture the data. A pencil should never be used.
- Corrections to source data should only be made at the time of original data capture or when other corroborating source documentation supports the edit.
- Corrections to source data should be lined-through, initialed, dated. White-out or other obliterating techniques should never be used.

EDC Reporting

Electronic Source Data for all subjects will be entered into *Dental Toolkit*. This is a secure, web-based EDC system, validated and US CFR Part 11 compliant provided by the GO Health Center.

Access to the EDC system shall be protected by login identification and password. All delegated Site personnel shall be trained on procedures for data entry into the web-based system prior to study start. Following, delegated staff shall be provided ID codes and passwords unique to each team member's delegated study role and blinding requirements. A staff member's ID code/password shall never be shared or used by another staff member, in any circumstance.

Data Quality Control

Data submitted to the EDC system must follow automated parameters programmed to ensure the collection of consistent and complete data. Clinical data for eligibility and safety will be calculated and verified via SAS programing. The project statistician and study coordinator may remotely review data listings generated at different time points during the study. Data queries may be generated to resolve any discrepancies or concerns. Submitted data as well as all data modifications to submitted data shall be documented in system audit trails.

Upon conclusion of the study, after all eCRFs are marked as complete and all discrepancies resolved, the Principal Investigator will be notified to review the case books. Once the Investigator has had time to review the case books, user privileges will be removed for all research personnel. Subsequently, the database shall be locked from all personnel other than the system administrator. The final data set shall be transferred to SAS and delivered via disk or into a protected file on a cloud server for the sponsor. A copy of the data shall be saved to a disk for archiving purposes, and be made available for any potential audits.

Study Design

It is planned that healthy volunteers will be consented and screened to enroll 53 subjects in order to complete with a minimum of 44 subjects (22 per treatment group). The following criteria must be met for subjects to qualify for enrollment:

Inclusion Criteria

Subjects accepted into the study must:

- INCL1 Be willing and physically able to carry out all study procedures and be available at all times required for participation
- INCL2 Be able to fully understand and comply with the written and verbal instructions provided
- INCL3 Provide written Informed Consent
- INCL4 Be age 18 – 70 years
- INCL5 Agree to return study materials at the required visit(s)
- INCL6 Have a minimum of 20 'scorable' teeth (excluding 3rd molars)

INCL7 Have more than or equal to 10% and less than or equal to 50% Bleeding on Probing (BOP) sites
INCL8 Have all PD less than or equal to 4mm
INCL10 Have at least 12 qualifying, interproximal units (3 per quadrant) with closed contacts, without crown or restorations. (See section 5.1.1 'Teeth Selection')
INCL11 Be a regular manual toothbrush user for at least 2 months.
INCL12 Be a non-smoker for at least 2 years.
INCL13 Be willing to abstain from use of chewing gum and consumption of apples, carrots or other hard crunchy foods or thick skinned fruits for 3-6 hours before each visit.
INCL14 Be willing to comply with 12-18 hours of no oral hygiene practices

Exclusion Criteria
Subjects shall be excluded if any of the following are present:

EXCL1 A Medical or Dental condition that would be unduly affected by participation in this study, per Investigator Discretion
EXCL2 Pregnant or nursing, per urine based pregnancy test
EXCL3 A medical condition requiring antibiotic pre-medication prior to dental appointments
EXCL4 Diagnosis of Xerostomia
EXCL5 Any oral or extra oral piercing that interferes with the ability to perform study procedures and/or clinical assessments in the mouth
EXCL6 Currently undergoing or requiring dental/periodontal treatment, or having had periodontal treatment in the six months preceding the study, where the subject's study participation could present an undue safety risk or obscure the evaluation of study endpoints, per Investigator /Examiner discretion
EXCL7 Oral surgery within the last 2 months
EXCL8 A known allergy or sensitivity to products planned for use in this study
EXCL9 Unwillingness to abstain from all other oral hygiene products other than those prescribed for the duration of the study
EXCL10 Participation in an oral care study within the previous 90 days
EXCL11 Are a dental student or dental professional
EXCL12 Diagnosed diabetes with a current (30 days) HbA1C greater than 7
EXCL13 Current use of antibiotic medications or use within 4 weeks of enrollment
EXCL14 Presence of heavy deposits of calculus, either supragingival and/or subgingival, per Investigator/Examiner discretion
EXCL15 Extensive crown or bridge work, rampant decay or excessive gingival recession, per Investigator/Examiner discretion
EXCL16 Presence of orthodontic bands interfering with efficacy outcome(s) per Investigator/Examiner discretion
EXCL17 Current use of professionally dispensed bleaching products or use within one month of screening.
EXCL18 Be an employee, spouse or a relative of an employee of the clinical research site, or a dental products manufacturing, research or marketing firm.
EXCL19 Chronic treatment (i.e., two weeks or more) with any medication known to affect periodontal status (e.g., phenytoin, calcium antagonists, cyclosporine,

anticoagulants, non-steroidal anti-inflammatory drugs) within one month of the screening examination (daily use of 81 mg Aspirin is not exclusionary)

EXCL20 Have any tooth sites with: ≥ 5mm PD or attachment loss ≥ 3mm, excluding 3rd molars

Continuation Criteria

Subjects who sign the informed consent form are screened for eligibility at Visit 1. Subjects meeting all enrollment criteria shall be enrolled into the study.

Withdrawal Criteria

Study participation is voluntary. The participant may refuse to consent or may withdraw from this study at any time without penalty or loss of benefits to which he/she is otherwise entitled. The Principal Investigator may terminate a study subject's participation in this study without his/her consent (e.g., for safety or significant non-compliance). Compensation for participation will be prorated for prematurely withdrawn subjects, (See Section 3.6 Products, Treatments and Medications not Permitted on Study

Treatment of Subjects

Subjects enrolled on the study are planned to complete 4 study visits as described below:

Schedule of Examinations and Tests

Visit 1 – Screening and Enrollment

Visit 1 shall be conducted in the following manner:

- *Informed Consent*

Potential subjects are given the most current IRB/EC-approved consent to read and are provided the opportunity to ask and have answered questions about the study. If they agree to participate, they shall sign the consent form and be given a copy for their records. Study procedures may then begin.

- *Medical/Dental History & Demographics*

The subject's medical and dental history and baseline health status (including baseline medications) shall be captured and screened by the investigator or designee against the eligibility criteria. Further, eligibility screening shall be assessed by participant interview, where appropriate. For safety monitoring, the baseline status shall be referenced when assessing for Adverse Events. A template of the medical/dental history form can be found in the Essential Documents File. Demographics (age, sex, race and ethnicity) shall also be collected.

- *Baseline Oral Examination*

A dental examiner shall perform an oral examination to note baseline anomalies for future safety assessments. The gingiva, buccal mucosa, lips, vestibule, palate, tongue, and floor of the mouth are examined. The oral cavity is carefully inspected for pathological conditions and other

abnormalities; e.g., evidence of gingival abrasion, irritations, lacerations, or ulcerations.

Additionally, teeth are examined to note the location and condition of all restorations, including, but not limited to: crowns (porcelain or metal), veneers, alloy restorations, composite restorations, etc.

- *Teeth Selection*

Twelve interproximal units shall be selected and qualified (3 units per quadrant) in order to collect MQH-PI and UNC-GI. All 12 interproximal units shall be sampled for MQH-PI and UNC GI to collect a total of 24 facial site scores.
The following are the selection qualifiers, for study teeth/sites

  - Qualifying units must include 1 anterior interproximal unit and 2 posterior interproximal units in each quadrant. (Two of the four posterior units must include a 1st molar and 2nd molar.)
  - Qualifying units must not include 3rd molars
  - Qualifying units must include teeth with closed contacts.
  - Qualifying units must include only natural dentition without dental restorations covering any portion of the mesiobuccal or distobuccal surfaces of the tooth.

- *Modified QH Plaque Index*
  A plaque assessment shall be assessed on teeth that make up the qualifying interproximal test sites using the Lobene - Turesky Modification of the Quigley-Hein Plaque Index(2). Plaque scores shall be visually assessed at the four (2) tooth surfaces that make up each of the 12 (6 per side) qualifying interproximal test units: mesiobuccal and distobuccal (scale of 0-5, see Table 1 footnotes for details).

- *UNC Gingival Index (UNC-GI)*
  A gingival assessment shall be performed based on the UNC modification of the Löe and Silness Gingival Index. The gingiva shall be assessed at **6 sites per tooth**: distobuccal, direct buccal, mesiobuccal, distolingual, direct lingual and mesiolingual surfaces.

Periodontal clinical measurements, including Peridodontal Probing Depth (PPD) and cementoenamel junction measures relative to the gingival margin (CEJ) and Bleeding on Probing (BOP) shall be assessed and reported per octant (quadrant 1 facial, quadrant 2 facial, quadrant 2 lingual, quadrant 1 lingual, quadrant 3 facial, quadrant 4 facial, quadrant 4 lingual, quadrant 3 lingual). The gingiva shall be gently dried and segmented into marginal and papillary units, **6 sites per tooth**: distobuccal, direct buccal, mesiobuccal, distolingual, direct lingual and mesiolingual surfaces. PPD shall be measured and recorded in tandem, at a site, before moving on to the next site within an octant. Once the PPD assessment is completed in an octant, BOP shall be assessed in the same site order in that

octant. Once all 3 measures have been collected in an octant, the process shall be repeated in the next octant until all octants have been assessed.

- *Probing Pocket Depth (PPD)*

  Full-mouth probing pockets depths shall be assessed at **6 sites per tooth** using a UNC15 periodontal probe (type to be used for all participants, all visits). PPD shall be measured from the free gingival margin to the base of the pocket and shall be recorded in millimeters (mm), rounding down to the nearest millimeter.

- *Bleeding on Probing (BOP)*

  A full mouth bleeding assessment shall be assessed at **6 sites per tooth**. A dichotomous index shall be used to record: bleeding (1), or the absence of bleeding (0).

- *Enrollment*

  Subjects who meet the eligibility criteria shall be enrolled. (Note: Eligibility criteria that require paper-based source documentation will be identified prior to study start (see section 3.11.1 for details)). The individual who confirms eligibility status to all criteria shall provide their signature/initials and date upon confirmation.

- *Prophylaxis and Referral for Care, if indicated*

  All subjects will be provided with dental prophylaxis. Any subject for whom a referral for urgent dental care is appropriate, will be provided these services.

- *Regime Product Dispense*

  All participants shall be dispensed the same oral hygiene products (Regimen 2- Twice daily use of: Oral-B Indicator manual toothbrush with Crest Cool Mint Gel dentifrice) in order to keep consistent during the study.

- *Supervised Regime Product Use*

  Participants shall demonstrate understanding of the brushing instructions in a supervised session. Research staff shall observe participants using their products to ensure proper usage according to instructions recommended by ADA, see Appendix I.

- *Follow-up Visit(s) Scheduled*

  The appointments for Visits 2 shall be scheduled. Plaque accumulation and diet restriction instructions, prior to the appointments, shall be reviewed. Additionally, participants shall be given verbal instructions to refrain from using prohibited treatments, medications and dental supplements for the duration of the study (see Section 3.6). Participants will be asked to provide preferred contact information (e.g. e-mail, phone or text) so that weekly visit reminders may be established.

Visit 2 – Baseline

Visit 2 shall occur 21 days after Visit 1 (+/- 3 days), in the following manner:

- *Randomization*

  Participants shall be assigned their treatment group, using a randomization list generated by UNC and provided to the GO Health Center unblinded study personnel prior to study activation. The Examiner(s) is blinded to which group each participant is assigned until conclusion of efficacy evaluations.

- *Plaque Accumulation*

  Participants shall be instructed to perform toothbrushing 12-18 hours prior to their scheduled appointment, and then refrain from all oral hygiene. A reminder message will be sent within 24 hours prior to the next scheduled study visit. This will allow for 12-18 hours of plaque accumulation. For example, if their appointment is on Monday, Jan 14th at 11:00am, the participant should brush on Sunday, January 13th between 7:00pm and 11:00pm with no brushing after 11:00pm. Actual accumulation shall be documented and any deviations reported.

- *Diet Restriction*

  Participants shall be instructed to refrain from use of chewing gum and consumption of apples, carrots or other hard crunchy foods or thick skinned fruits during the plaque accumulation period (3-6 hours prior to their study visits).

- *Adverse Event Monitoring: Oral Exam*

  An oral examination is conducted as described in Section 5.1.1. Any adverse change(s) in the mouth are to be documented as Adverse Event(s). See Section 7.0 for details.

- *Modified QH Plaque Index*

  A designated-site plaque index shall be performed as described in Section 5.1.1.

- *UNC Gingival Index*

  A designated-site gingival index shall be performed as described in Section 5.1.1.

- *Probing Pocket Depth (PPD) & CEJ*

  A designated-site probing pocket depth shall be performed as described in Section 5.1.1.

- *Bleeding on Probing (BOP)*

  A designated-site bleeding assessment shall be performed as described in Section 5.1.1.

- *Treatment Product Dispense*
  Participants shall be dispensed the appropriate treatment products according to their randomization assignment. Participants will receive either: GUM Soft-Picks® Advanced or Oral-B Pro-Health Glide Original floss

- *Treatment Product Usage Instruction*
  Participants shall be provided the appropriate written instructions with detailed review of product use by the research staff. See Appendices II and III.

- *Supervised Treatment Product Use*
  Participants shall demonstrate understanding of the interdental cleaning instructions in a supervised session. Research staff shall observe participants using their dispensed products to ensure proper usage according to instructions.

- *Issue Subject Diary*
  Participants are provided an at-home user experience diary, as well as his/her compliance diary. Participants shall be instructed on proper completion by the designated research staff. The diary should indicate the level of motivation to use the product and end satisfaction for each encounter. A template of the diary can be found in Appendix IV.

- *Follow-up Visit(s) Scheduled*
  The appointment for Visit 3 shall be scheduled. Plaque accumulation and diet restriction instructions that apply to the next scheduled appointment shall be reviewed. Additionally, participants shall be given verbal instructions to refrain from using prohibited treatments, medications and dental supplements for the duration of the study (see Section 3.6). Study visit appointment reminders will be sent within 24 hours prior to the next scheduled study visits.

Visit 3– Day 14

Visit 3 shall occur 14 days after Visit 2 (+/- 2 days), in the following manner:

- *Plaque Accumulation*
  Participants shall be instructed to perform their last brushing 12-18 hours prior to their scheduled appointment as described in Section 5.1.2. The actual accumulation shall be documented and any deviations reported.

  - *Diet Restriction*

  Participants shall be instructed to refrain from use of chewing gum and consumption of apples, carrots or other hard crunchy foods or thick skinned fruits during the plaque accumulation period (3-6 hours prior to their appointment).

- *Compliance Monitoring*
  The research staff performs a compliance check with a verbal interview and review of the diary to determine if the subject has followed study instructions.

Any non-compliance to requirements (see Section 5.2) is to be documented as a protocol deviation(s).

- *Adverse Events Monitoring: Interview and Health History Update*
  The research staff research staff and/or dental examiner shall review with the participants their medical/dental status, health history and medications and compare to baseline for any potential adverse changes. See Section 7.0 for details on reportable Adverse Events.

- *Adverse Event Monitoring: Oral Exam*
  An oral examination is conducted as described in Section 5.1.1. Any adverse change(s) in the mouth are to be documented as Adverse Event(s). See Section 7.0 for details.

- *Modified QH Plaque Index*
  A designated-site plaque index shall be performed as described in Section 5.1.1.

  - *UNC Gingival Index*

  A designated-site gingival index shall be performed as described in Section 5.1.1.

- *Follow-up Visit(s) Scheduled*
  The appointments for Visits 4 shall be scheduled. Plaque accumulation and diet restriction instructions, prior to the appointments, shall be reviewed. Additionally, subjects shall be given verbal instructions to refrain from using prohibited treatments, medications and dental supplements for the duration of the study (see Section 3.6). Lastly, participants shall be informed to return with their study diary.

Visit 4– Day 28, Final

Visit 4 shall occur 28 days after Visit 2 (+/- 2 days), in the following manner:

- *Plaque Accumulation*
  Participants shall be instructed to perform their last brushing 12-18 hours prior to their scheduled appointment as described in Section 5.1.2. The actual accumulation shall be documented and any deviations reported.

- *Diet Restriction*
  Participants shall be instructed to refrain from use of chewing gum and consumption of apples, carrots or other hard crunchy foods or thick skinned fruits during the plaque accumulation period (3-6 hours prior to their appointment).

- *Compliance Monitoring*
  Research staff will perform a compliance check with a verbal interview and review of the diary to determine if the subject has followed study instructions. Any non-compliance to requirements (see Section 5.2) is to be documented as a protocol deviation(s).

- *Adverse Events Monitoring: Interview and Health History Update*
  Research staff and/or the dental examiner shall review with the participants their medical/dental status, health history and medications and compare to baseline for any potential adverse changes. See Section 7.0 for details on reportable Adverse Events.

- *Adverse Event Monitoring: Oral Exam*
  An oral examination is conducted as described in Section 5.1.1. Any adverse change(s) in the mouth are to be documented as Adverse Event(s). See Section 7.0 for details.

- *Modified QH Plaque Index*
  A designated-site plaque index shall be performed as described in Section 5.1.1.

- *UNC Gingival Index*
  A designated-site gingival index shall be performed as described in Section 5.1.1.

- *Probing Pocket Depth (PPD) & CEJ*
  A full mouth probing pocket depth and CEJ measures shall be performed as described in visit 1.

- *Bleeding on Probing (BOP)*
  A full mouth bleeding assessment shall be performed as described in visit 1.

- *Prophylaxis and Referral for Care, if indicated*
  At the discretion of the Examiner, any subject for whom a referral to additional dental care, or for whom a prophylaxis is appropriate, is provided these services.

- *Product Return*
  Participants shall return study diary and any unused study products. Report any forgotten product(s) as a protocol deviation. If the diary is forgotten, remind the participant to return with the diary as soon as conveniently possible.

- *Subject Questionnaire*
  All participants are provided a questionnaire and shall be instructed on proper completion by the designated research staff . The questionnaire should indicate the level of product familiarity, overall usage satisfaction, as well as

motivation to use the product in the future. A template of the questionnaire can be found in Appendix V.

- *Subject Compensation*
  All participants that sign the informed consent, whether they complete the study or not, shall be reimbursed according to the schedule outlined in the IRB/EC-approved Informed Consent Form.

- *Subject Dismissed*
  Subjects are dismissed from the study. See Section 7.0 in the event of an ongoing Adverse Event at the time of dismissal.

Visit Overview Table

Table 1 provides an overview of Visits and Study Procedures:

Procedure	Performed by:	Visit			
		1 Screening	2 Day 0	3 Day 12	4 Day 28
Plaque Accumulation	Participant	X	X	X	X
Diet Restriction	Participant	X	X	X	X
Informed Consent	Study Coordinator/ Research Staff	X			
Medical/Dental History & Demographics	Examiner/ Designee	X			
Compliance Monitoring	Coordinator/Research Staff			X	X
AE Monitoring: Interview	Coordinator/Research Staff	X	X	X	X
Baseline Oral Exam	Examiner		X		
AE Monitoring: Oral Exam	Blinded Examiner	X*	X	X	X
Teeth Selection	Examiner	X			
Modified QH Plaque Index[A]	Blinded Examiner	X*	X	X	X
UNC Gingival Index	Blinded Examiner	X*	X[B]	X[B]	X[B]
Pocket Probing Depth & CEJ[C]	Blinded Examiner	X*	X		X
Bleeding on Probing[D]	Blinded Examiner	X*	X		X
Enrollment	Study Coordinator/ Research Staff	X			
Randomization	Study Coordinator/ Unblinded Research Staff		X		
Product Dispense with Usage Instruction	Coordinator/Unblinded Research Staff	X	X		
Supervised Product Use	Coordinator/Unblinded Research Staff	X	X		
Issue Subject Diary	Coordinator/Unblinded Research Staff		X		
Follow-up Visits Scheduled	Research Staff	X	X	X	
Follow Up Visit Reminders	Research Staff	X	X	X	
Prophylaxis and/or Referral for Care, if indicated	Treatment Provider	X			X
Questionnaire	Participant				X
Compliance Review & Subject Compensation	Study Coordinator/Research Assistant		X	X	X

***** Blinding not required during visit 1 clinical indices

[A]**Modified QH Plaque Index (**Lobene - Turesky Modification of the Quigley-Hein Plaque Index) reference # 2 - Dental Plaque and debris will be graded using the same scale as the Turesky Index, but only at the two (2) sites that make up each of the 12 (3 per quadrant) qualifying interproximal units: mesiobuccal and distobuccal surfaces. The area to be graded on the mesial and distal will be determined by three reference points. These points are the line angle of the tooth to the contact point both

bordered by the gingival margin. This allows a small triangular area to be graded. In the event that there is no contact between teeth, the height of contour of the tooth should be used as the reference point.

0 =No debris or stain present on the clinical crown.
1=Presence of a discontinuous line of plaque at the gingival margin
2=A continuous line of plaque at the gingival margin which does not extend greater than 1 mm from the margin
3=Plaque coverage which is greater than 1 mm but does not extend more than one third of the tooth
4=Plaque which covers more than one third but not more than two third of the tooth surface
5=Plaque coverage over more than two third of the tooth surface

[B] **UNC Gingival Index**: - grading will include only the two (2) sites that make up each of the 12 (3 per quadrant) qualifying interproximal units: mesiobuccal and distobuccal surfaces.
0 =Normal gingiva (pink, firm, stippled),
1 =Mild inflammation: slight change in color, slight edema, no bleeding on probing,
2 =Moderate inflammation: glazing, redness, edema, bleeding on probing,
3 =Severe inflammation: marked redness and edema, ulceration, tendency to spontaneous bleeding

[C] **Pocket Probing Depth & CEJ**: **-** Full mouth (excluding 3rd molars); 6 sites per tooth: distobuccal, distal, mesiobuccal, and distolingual, lingual and mesiolingual surfaces: **(mm)**

[D]**Bleeding on Probing -** Full mouth (excluding 3rd molars); 6 sites per tooth: distobuccal, distal, mesiobuccal, and distolingual, lingual and mesiolingual surfaces, except for last site in each arch:
0 =No bleeding within 10 seconds after probing.
1 =Bleeding within 10 seconds after probing.

Procedures for Monitoring Compliance
Completion of all study procedures, both site-performed and subject-performed, shall be source documented, either on paper or directly in the EDC system (see Section 3.11).

At Visit 1, participants' medical/dental status shall be documented.

At the follow-up visit(s), the medical/dental status shall be reviewed with the participant for any changes to health, medications, therapies or treatments. Additionally, the participant's diary shall be reviewed for at home product use.

All non-compliance to protocol procedures shall be reported as protocol deviation(s). Examples of non-compliance include, but are not limited to:

Participant Non-Compliance
- failure to follow brushing instruction
- failure to complete study diary
- failure to follow plaque accumulation instruction
- prohibited medication usage
- prohibited oral care product usage
- failure to return product

General Non-Compliance
- mis-randomization*
- wrong product dispensed
- failure to supervise brushing or any other missed procedure
- subject return visit outside of protocol window
- enrollment of ineligible subject*
- Interval of non-compliance

Significant non-compliance (marked above with an '*', or other non-compliance that may affect study integrity (e.g., a participant did not perform 'most all' of the at-home product usage procedures, participant received prohibited dental treatment, etc.)), shall be reported immediately to the Sponsor as well as the Principal Investigator.

Product Accountability
Receipt and return/disposition of all study products (from and to the Sponsor) shall be tracked on Accountability records provided by the Sponsor. Upon receipt, product shipments shall be inventoried and written, dated confirmation provided on the Accountability records. A copy shall be provided to the Sponsor by fax or scanned into emails.

Product dispense, return and disposition (to and from study subjects) shall be documented. The procedure for documentation shall be determined prior to commencement of the study.

At the conclusion of the study, all unused provided products by the Sponsor must be returned to the Sponsor. The date of shipment return shall be reported on the accountability form. Once all returnable products are reconciled and accounted for they can be returned to Sunstar Americas, Inc. via FedEx using account [redacted] to at:

Attention: Akane Takemura
Sunstar Americas, Inc.
301 E. Central Rd.
Schaumburg, IL 60195

Efficacy Assessments

Parameters of Efficacy

The primary efficacy measure for this study is reduction in interproximal plaque accumulation from baseline as evaluated by the MQH-PI following 14 (2 weeks) and 28 days (4 weeks) of home-use. MQH-PI will be assessed by the mean change and percent reduction from baseline (Visit 2) to post 14 days (Visit 3) and 28 days (Visit 4) of home use in plaque index score. A designated site plaque assessment shall be performed using the Lobene - Turesky Modification of the Quigley-Hein Plaque Index. Plaque removal will be summarized overall and by region (i.e. anterior interproximal and posterior interproximal). Overall and for each region, plaque score will be calculated as the total number of sites classified as having plaque present divided by total number of evaluable sites.

Secondary efficacy parameter is reduction in gingival inflammation from baseline as evaluated by the UNC-GI, PPD and BOP following 28 days (4 weeks) of home-use. UNC-GI score will be calculated as the sum of scores of all evaluable sites divided by the number of evaluable sites. UNC-GI score will be expressed as the raw average score for a subject, as a reduction from baseline (baseline score minus post-baseline score), and as percent reduction calculated as the reduction in UNC-GI score divided by the baseline UNC-GI score times 100. Same score evaluation will be performed for PPD and BOP, which is baseline score minus post-baseline score, and as for calculating percent reduction, the reduction in PPD/BOP score will be divided by the baseline PPD/BOP score times 100.

Methods and Timing of Assessing and Analyzing Efficacy Variables

MQH-PI, UNC-GI, PPD and BOP will be assessed at baseline (i.e., Study Visit 2), post 14 and 28 days for MQH-PI, and only post 28 days for all other indices, of home use (i.e., Study Visits 3 and Visit 4). Participants will be instructed to abstain from brushing 12-18 hours prior to their scheduled appointment. A trained and calibrated examiner shall perform all clinical evaluations.

Safety Assessments

Participant safety shall be monitored from the time each subject signs the Informed Consent Form until conclusion of the study. Any event, however, that is a UADE (see Section 7.2) in the opinion of the investigator is to be followed until resolution (see Section 7.6). Subject safety shall be monitored to detect any deviations in the medical/dental status present at baseline.

Concomitant Medications
At Visit 1, baseline concomitant medications shall be source documented and reviewed by the Investigator/Examiner against eligibility criteria. Only changes to baseline medications (i.e., changes to amount, frequency, etc.) or new medications require reporting in the CRFs. Changes shall be reviewed with the Investigator/ and study coordinator for 'reportable' Adverse Events.

Adverse Events
At Visit 1, a medical/dental history form is provided to each participant and is reviewed with the participant by the Investigator/Examiner to establish baseline health status. Relevant historical and current health information is noted. Additionally, an oral exam further identifies baseline dental status. At all subsequent study visits, adverse changes from the baseline medical/dental status of each participant is assessed via participant interview, diary review, oral exams, etc. The subject may report adverse events and changes to con meds by phone or other means of communications at any time until conclusion of the study.

The following adverse changes from baseline require reporting as Adverse Events in the eCRFs:

- Any adverse change that has either of the following relations to the test products or study procedures: 'possibly related' or 'related'
- Any adverse change which occurs in/around the oral cavity, regardless of relationship status
- Any event that is an Unanticipated Adverse Device Effect (UADE, see section 7.2)

An adverse change that does not meet any of the above does not require reporting to the Sponsor (or the CRFs).

Examples of reportable AEs and non-reportable AEs include, but are not limited to:

Reportable AEs
- abrasion in /around the oral cavity
- lost tooth
- tooth sensitivity
- mucosal fibroma
- noticeable increase in gingival inflammation
- oral ulceration
- palatal burn
- gum irritation / soreness
- papilla laceration / trauma
- damaged restoration

Non-reportable AEs
- broken bone
- cold symptoms
- headache, if it isn't at least possibly related to study participation
- infection, if it isn't at least possibly related to study participation
- cold sore
- cheek bite
- linea alba
- loosened filling
- dry or cracked lips

Unanticipated Adverse Device Effects
A UADE is defined in the United States 21 Code of Federal Regulations Part 812.3(s) as "any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects".

Other important medical events which may not result in any of the outcomes above, but which may require intervention to prevent one of the outcomes above, may in the opinion of the investigator, be considered a UADE.

Any UADE requires immediate reporting to the Sponsor upon discovery:

Contact: Akane Takemura
E-mail: akane.takemura@us.sunstar.com
Tel: 847-794-4276

Parameters of Safety
Parameters of safety include reportable (see Section 7.1) adverse changes in the medical and/or dental status of the subject from the time of assignment of investigational products until completion of the study or resolution of the event, as appropriate. Additional parameters of safety include review of concomitant medications and deviation or violations from the protocol for each participant.

Methods and Timing of Assessing and Analyzing Safety Variables
Safety variables are assessed in a verbal interview and examinations at each follow-up study visit in which the participant's current medical and dental status is reviewed compared to baseline, and a determination is made about the relation of any events to the study participation. In addition, the oral examination conducted at these visits is also used to screen for adverse events with relevant safety information recorded. Lastly, any

adverse event reported by a subject in between visits is assessed upon reporting as described above.

Procedures for Reporting Safety Events
Reportable Adverse Events, as described in Section 7.1, shall be recorded in the eCRFs, and an assessment shall be made by the Principal Investigator/designee of the following metrics for each event: severity, serious, anticipated (if serious), relation (to study participation and device), action taken and outcome. Options for each of these metrics can be found in the Source Document Template Adverse Events Log form.

Expedited Reporting
All adverse events that are serious and occurring in the mouth; or serious and at least possibly related to the study, as well as all UADEs (see Section 7.2) are to be reported to the Sponsor within 24 hours of the investigator learning of the event.

Contact: Akane Takemura
E-mail: akane.takemura@us.sunstar.com
Tel: 847-794-4276

The Principal Investigator is responsible for reporting the event to the appropriate IRB/EC as dictated by the guidelines defined by the IRB/EC.

Other Reporting
All other safety events that do not meet the expedited reporting criteria as described above are collected at the time of reporting by the participant, or detection by the investigator. They are recorded and maintained as part of the study record and reported to the Sponsor via the eCRF.

The disposition of all safety events, assignment of relatedness, seriousness is the responsibility of the Principal Investigator.

Disposition and Follow-up of Adverse Events
An adverse event that is present at the time of study completion is to be designated as ongoing on the eCRF (i.e., 'Recovering/Resolving' or 'Not Recovered/Not Resolved'). However, all ongoing events that require expedited reporting, as described in Section 7.5, or other important medical findings, per the opinion of the investigator, are to be followed until resolution.

Statistical and Analytical Plan

Determination of Sample Size
The primary endpoint of this study is to distinguish the difference in measured interproximal plaque indices between two treatment groups after 14-day and 28-day of using a different kind of interproximal cleaning device. Therefore the determination of sample size is based on the following equation and parameters [1]:

$$n = \frac{2[(a+b)^2\sigma^2]}{(\mu_1 - \mu_2)}$$

Where:

n = the sample size in each of the groups
μ_1 = population mean in treatment Group A
μ_2 = population mean in treatment Group B
$\mu_1 - \mu_2$ = the difference the investigator wishes to detect
σ^2 = estimated standard deviation
a = conventional multiplier for alpha (type I error)
b = conventional multiplier for power (type II error)

The value of the difference between two treatment groups ($\mu_1 - \mu_2$) was referenced from the similar clinical study focused on plaque accumulation reduction by using different types of interproximal cleaning devices[2]. It was determined when the value of the difference between two groups was 0.25 based on the fact that the measured difference between an interdental brush and floss was larger (>0.30 at week 6) in the mentioned clinical study[2].

By substituting all parameters with follows, the value of sample size n becomes: n = 33:

($\mu_1 - \mu_2$)	0.25
σ^2	$(0.25)^2 = 0.0625$
a	1.96 (for 95% confidence intervals (CI))
b	1.28 (90% power)
n	**22**

[1] Noordzij M, Tripepi G, Dekker FW, *et al*. Sample size calculations: basic principles and common pitfalls. *Nephrol Dial Transplant* 2010;25:1388-1393.
[2] Jackson MA, Kellett M, Worthington HV, *et al*. Comparison of interdental cleaning methods: a randomized controlled trial. *J Periodontol* 2006;77:1421-1429.

General Considerations

The primary analysis will be performed including all randomized subjects with a baseline and post Day 14 and Day 28 (i.e., Visit 3 and Visit 4) efficacy evaluation (modified intent to treat, MITT). Subjects with a compliance level of 75% will be grouped according to the randomized treatment assignment. The analysis of safety will include all randomized subjects who were exposed to treatment.

All variables will be summarized by descriptive statistics. The statistics for continuous variables include: number of observations, mean, median, and standard deviation, minimum, maximum and 95% confidence intervals (CIs). For categorical variables, number and percentage of subjects with the event will be presented.

All analyses will be conducted using SAS® or equivalent software

Subject Disposition
Participant disposition, including the total number of participants enrolled, randomized, completed, early terminations and withdrawals, will be presented by study visit, treatment group, and overall. In addition, a listing will be provided with the reasons for discontinuation by treatment group.

Demographics and Baseline Characteristics
Standard subject demographics (e.g., age, sex, race and ethnicity) and baseline characteristics (e.g., number of missing teeth, plaque score, etc.) will be summarized for all participants randomized and for MITT subjects. For continuous participant characteristics, means will be compared using one way analysis of variance (ANOVA). The incidence of the categorical variables will be compared using the Chi-square test or Fisher's exact test as appropriate.

All summaries will be presented by treatment group and overall. In addition, baseline characteristics will be summarized by treatment group and sex.

Treatment Compliance
Participant compliance will be listed by treatment group. If applicable, comparability between the treatment groups will be evaluated using a Chi-square or Fisher's exact test as appropriate for categorical variables, and one way ANOVA for continuous variables. A listing of all deviations will be presented.

Primary Efficacy Analysis
The primary efficacy measure for this study is reduction in plaque index as evaluated by MQH-PI following 14 days (2 weeks) and 28 days (4 weeks) of home use. MQH-PI score will be considered as continuous variable and will be calculated as the sum of scores of all evaluable sites divided by the number of evaluable sites. MQH-PI score will be expressed as the raw average score for a participant, as a reduction from baseline (baseline score minus post-baseline score), and as percent reduction calculated as the reduction in MQH-PI score divided by the baseline MQH-PI score times 100.

The following hypothesis will be tested:

$$H_o: U_{MQHPI\text{-}SP} - U_{MPI\text{-}floss} = 0$$
$$H_A: U_{MQHPI\text{-}SP} - U_{MPI\text{-}floss} \neq 0$$

The primary analysis will be done on a modified ITT basis including all participants with baseline and post baseline efficacy evaluation as follows:
$Y_{ij} = \mu + b_i + \lambda_j + \varepsilon_{ij}$

Where:
Y_{ijk} denotes the overall change (or percent reduction) in MQH-PI for the participant i, treatment j, i = 1,2,…, N; j = 1,2,3,4.

μ denotes the overall mean.
b_i denotes the baseline efficacy level corresponding to i^{th} subject.
λ_j denotes the fixed effect corresponding to the j^{th} treatment.

ε_{ij} denotes the unexplained or residual variation.

In addition, the following assumptions will be made:
$\varepsilon_{ij} \sim N(0,\sigma^2)$ for all i=1, 2,…,N; for all j = 1,2,...M; where N denotes the total number of participants , M denotes the total number of treatments.

Analysis of the statistical model above will be performed using Mixed model. If the required assumptions for the mixed model are violated, transformation of the data or non-parametric procedures may be used. Superiority will be declared based on the F-test. In addition, least square means (LSM) and 95% confidence interval for the means will be presented.

Supplementary analyses will be performed with sex as a covariate in the model. Least squares means, SEs of the least square means, and two-sided 95% CIs will be presented by treatment group and sex.

Secondary Efficacy Analysis
The secondary efficacy measure for this study is the reduction from baseline for UNC-GI and BOP (after 28 days). UNC-GI will be calculated as described above. BOP will be calculated as the number of sites classified as having bleeding present divided by the number of evaluable sites. BOP score will be expressed as the raw average score for a participant, as a reduction from baseline to post 28 days of home use, and as percent reduction calculated as the reduction in BOP score divided by the baseline BOP score times 100. Additionally, the number and percent of bleeding sites will be evaluated. Any site with a BOP score =1 will be counted as a bleeding site. The percent of sites bleeding will be calculated as the number of sites with BOP score =1 divided by the number of evaluable sites times 100.

The secondary analysis will include all randomized participants with a baseline and a post baseline evaluation for the parameter of interest. A statistical model similar to the primary analysis will be used to generate LS means, SEs for the least square means, and two-sided 95% CIs. In addition, PPD will be analyzed using 28 days as repeated measure over time.

Supplementary analyses will be performed with sex as a covariate in the model. Least squares means, SEs of the means, and two-sided 95% CIs will be presented by treatment group and gender. In addition all primary and secondary endpoints will be analyzed using a repeated measure approach.

Safety Analysis
Adverse events and oral examination abnormalities will be presented in data listings.

Interim Analysis
There is no interim analysis planned for this study.

Access to Source Documents

This study will be monitored to ensure that documents used to originally record participant data (source documents) are maintained, and to verify that transcribed data are accurately reflected on the study electronic Case Report Forms. Source documentation must be maintained in a secure area. Study-specific source documentation shall have limited access to Investigator-delegated study staff. Until all study procedures are performed, no blinded study staff shall have access to source documentation which may indicates product assignment or efficacy outcomes. All source documentation must be made available for review by Sponsor or its designees as well as regulatory agencies.

Ethical Considerations

All participants enrolled on this study shall receive an oral hygiene regimen that is, at minimum, considered standard of care. There is no placebo offered in this trial and no participant shall therefore forego general dental hygiene. The ethical principles for the treatment of human participants on this study have their origin in the Declaration of Helsinki. This protocol must be reviewed and approved by an authorized IRB/EC prior to its implementation. Any amendments to the protocol must be reviewed and approved by the study Sponsor, and subsequently, by the designated IRB/EC, according to the approval committee's requirements.

Study Confidentiality

Study records, including each participant's signed informed consent, and other study-related documents pertaining to the conduct of the study shall be kept in a secure area. Confidentiality shall be maintained. The results of this research project may be presented at meetings or in publications; however, subject identity will not be disclosed in such publications.

Confidentiality Standards
This protocol, test-methodology, study products, the study data and data management system contain confidential and proprietary information. Release of such information outside the scope of planned study operation is prohibited.

Participant Confidentiality
Participants enrolled on study shall be assigned a study ID code. All recorded data are then entered per the unique Subject ID. Study data available to the Sponsor are thus a 'coded' data set. Participant information shall remain confidential. However, consent forms and dental records that identify participants may be inspected by the sponsor, its authorized designees and regulatory agencies including but not limited to, the Department of Health and Human Services (DHHS), the United States Food and Drug Administration (FDA), other foreign regulatory bodies and the Institutional Review Board/Ethics Committee for this study. Because of the need to release information to these parties, absolute confidentiality cannot be guaranteed. Only authorized personnel associated with the conduct and/or review of the study and the resultant data shall have access to information that links subject identifiers to the corresponding assigned study code. Disclosure of subject information beyond the above mentioned representatives and agencies is prohibited.

Financial Considerations

Each participant shall receive compensation as designated in the IRB/EC approved Informed Consent Form. In the event that a participant withdraws or is removed from the study, compensation shall be pro-rated appropriately, as defined in the Informed Consent Form.

Publication Policy

The rights for publication of results from this study are at the coordination discretion of Sponsor and UNC. The Investigator must request permission from Sponsor prior to initiating any publication. Permission must be requested and received in writing. Review and approval of any data, abstract or manuscript is required. Sponsor reserves the right to review any presentation of study methodology, data collection, data analysis, interpretation of data, proprietary information or patented technology.

Investigator's Statement

I agree to conduct the trial as outlined in the protocol in accordance with the Sponsor's guidelines and other applicable FDA regulations, and conditions of approval imposed by the reviewing IRB. The Sponsor's guidelines include, but are not limited to:

- Provide Sunstar Americas Inc. selected representative with current curriculum vitae including a statement regarding relevant experience.
- Provide supervision of all device testing involving human subjects.
- Permission to allow Sunstar Amercias, Inc. and/or regulatory agencies to inspect study facilities and pertinent records at reasonable times and in a reasonable manner that ensures subject confidentiality.
- Submission of the proposed clinical investigation including the protocol and the consent form to an IRB for approval and the acquisition of written approval for each subject ensuring that the requirements for obtaining informed consent are obtained prior to the use of any test articles.
- Submission of any significant deviations from the protocol to the IRB and the sponsor. Any proposed changes or deviations from the protocol require that the informed consent also reflects such changes or deviations and that the revised informed consent be approved by an IRB.
- Documentation and explanation of individual protocol deviations and violations are captured with explanations as indicated.
- Submission of reports of Adverse Events to the Sponsor and IRB as outlined in the protocol.
- Submission of timely progress reports to the IRB and Sponsor at appropriate intervals on a schedule determined by the IRB or Sponsor, as indicated.
- Record keeping: the Investigator shall maintain adequate and accurate records designed to record completion of all study procedures, related observations and other key data (such as safety, compliance and product accountability) pertinent to the investigation on each subject enrolled. The investigator must maintain these records for a period of 10 years following completion of the study report and related publications.

I agree that all information provided to me by the Sponsor including pre-clinical data, protocols, electronic databases, CRFs, and verbal and written information shall be kept strictly confidential and confined to the clinical personnel involved in conduct of the trial. It is recognized that this information may be related in confidence to the IRB/EC. I also understand that reports or information about the trial or its progress shall not be provided to anyone not involved in the trial other than the Sponsor or other legally constituted authority.

_____ _____

Principal Investigator's Signature Date

_Antonio J. Moretti_____

Principal Investigator's Printed Name

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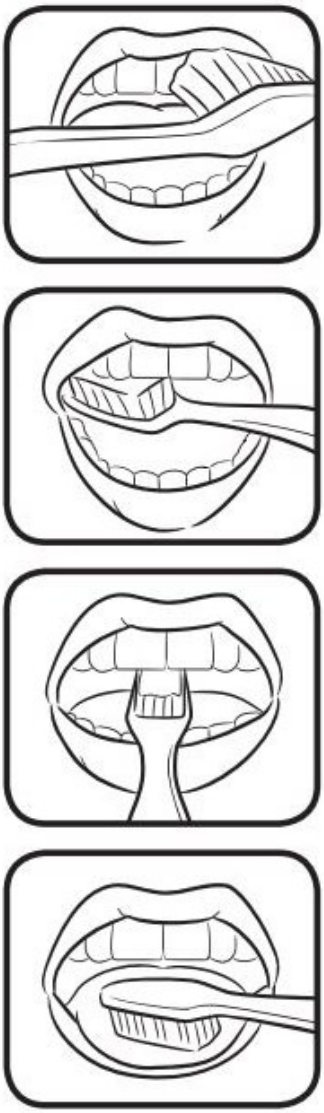
Appendix I **Product Instruction for tooth brushing (by ADA)**

How to Brush



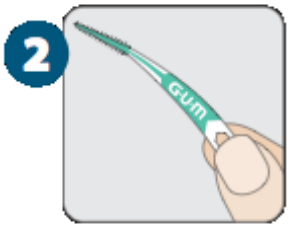
- Place the toothbrush at a 45-degree angle to the gums.
- Move the brush back and forth gently in short strokes.
- Brush the outer surfaces, the inside surfaces and the chewing surfaces of all teeth.
- To clean the inside surface of the front teeth, tilt the brush vertically and make several up-and-down strokes.
- Brush your tongue to remove bacteria and keep your breath fresh.

Appendix II **Product Instruction for GUM Soft-Picks® Advanced**

Product Instruction – How to use

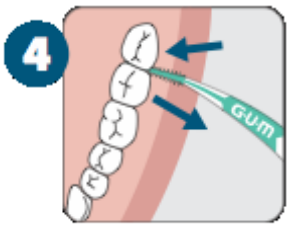
Soft-Picks® Advanced

Use a pick while looking into a mirror.



Hold the pick behind G·U·M® logo (where holes are present) with your thumb and index finger.

Slowly slide the pick between two teeth from your cheek side, so as not to damage the gum.



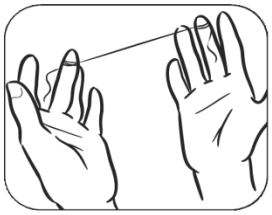
While holding the pick horizontally, move it back and forth along the tooth surface for 3 times (1 time = the tip goes between teeth and then pulled out).

If a tip of pick gets bent, please use a new pick.

Discard the pick.

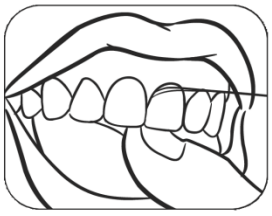
Appendix III Product Instruction for Glide Pro-Health Floss

How to Floss



- Use about 18 inches of floss wound around one of your middle fingers, with the rest wound around the opposite middle finger.

- Hold the floss tightly between the thumbs and forefingers and gently insert it between the teeth.



- Curve the floss into a "C" shape against the side of the tooth.

- Rub the floss gently up and down, keeping it pressed against the tooth. Don't jerk or snap the floss.

- Floss all your teeth. Don't forget to floss behind your back teeth.

Appendix IV Template of a User Diary (only Day 1)

User Diary

Instructions

1. Please answer your question before and after cleaning your teeth for the duration of this study.
2. Please provide your response by checking the circle.
3. If you would like to make comments about the assigned product, as well as your medication and health condition, please write on the bottom section of a page called "Memo".

MEDICATION FORM

Name of the Medication	**Reason Taken**	**Dosage**	**Date Started** (mm / dd/ yyyy)	**Date Stopped** (mm / dd/ yyyy)
e.g. Tylenol	Headache	1 tab / 3 times / day	7/28/2016	7/28/2016
Comments:				

User Diary - Day 1

◯ Yes, I used the assigned product.

◯ No, I didn't use the assigned product.

Before Cleaning *(Please check your responses)*

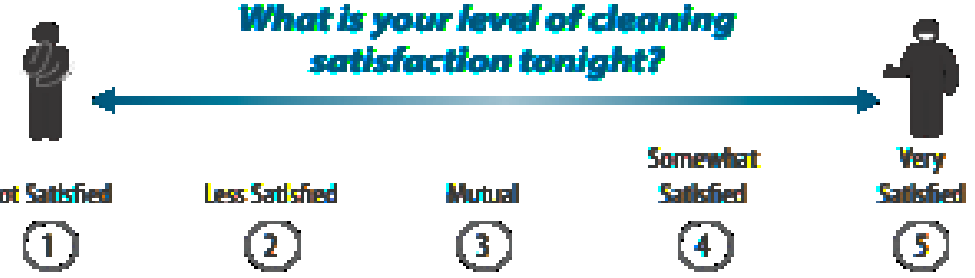
What is your motivation level to clean your teeth tonight?

Memo: _____

User Diary - Day 1

After Cleaning *(Please check your responses)*

Did you discard the assigned product? ◯ Yes ◯ No



Memo: _____

Appendix V **User Questionnaire**

For each statement, please describe how important it is to you when choosing a product for between teeth cleaning, using the following scale:

	Not At All Important	Not Very Important	Somewhat Important	Very Important	Extremely Important
	1	2	3	4	5
Removes food and debris from between teeth					
Provides a thorough clean between teeth					
Fits easily between my teeth					
Is easy to clean back teeth					
Makes between teeth cleaning quick					
Makes between teeth cleaning easy					
Makes between teeth cleaning convenient					
Is easy to hold during use					
Feels comfortable during use					
Makes my mouth feel fresh					
Is easy to understand how to use correctly					
Makes my mouth feel clean					
Are easy to use out of the home					
Is pleasant to use					
Cleans easily around crowns and bridges					

Please indicate how much you agree that each of the following characteristics accurately describes the product you used during this study:

	Disagree Strongly	Disagree Somewhat	Agree nor Disagree	Agree Somewhat	Agree Strongly
	1	2	3	4	5
Removes food and debris from between teeth					
Provides a thorough clean between teeth					
Fits easily between my teeth					
Is easy to clean back teeth					
Makes between teeth cleaning quick					
Makes between teeth cleaning easy					
Makes between teeth cleaning convenient					
Is easy to hold during use					
Is difficult to use					
Feels comfortable during use					
Makes my mouth feel fresh					
Is easy to understand how to use correctly					
Makes my mouth feel clean					
Are easy to use out of the home					
Is pleasant to use					
Cleans easily around crowns and bridges					