GlaxoSmithKline
Consumer Healthcare

STATISTICAL REPORTING AND ANALYSIS PLAN

A RANDOMIZED, EXAMINER BLIND, CROSSOVER, *IN SITU* EROSION STUDY TO INVESTIGATE THE EFFICACY OF AN EXPERIMENTAL DENTIFRICE IN REMINERALIZATION OF PREVIOUSLY SOFTENED ENAMEL COMPARED TO PLACEBO DENTIFRICE

Protocol Number: 208166

Phase: 3

Template Version Effective: 15-Jul-2017

Document History

Document	Version Date	Summary of Changes (New analysis or Change in planned analysis)
Amendment 1	27-Feb-2018	Blinded data review of surface micro hardness data helped to identify a discrepancy between clinical protocol and analytical protocol. Following that identification, an administrative letter (#3-22FEB2018) was issued to correct that discrepancy. Therefore, 208166 Statistical Report and Analysis Plan is amended to reflect this administrative change. The following text from section 4.4.1.2 will be amended: **Old text:** The baseline surface micro hardness and first demineralization level (E1) will not be included in the model as covariates as the samples will be preselected so that each sample has a measurement of 43 +/-3 µm (at baseline, B) **and 120 ± 20 µm (after the first erosive challenge, E1).** **New text:** The baseline surface micro hardness and first demineralization level will not be included in the model as covariates as the samples will be preselected so that each sample has a measurement of 43 +/-3 µm at baseline (B**) and 10-20 µm greater than the baseline after the first erosive challenge (E1).**
Analysis Plan	20-Dec-2017	Not applicable (N/A)

Amendments incorporate all revisions to date.

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Glossary

AE	adverse event
ARR	acid resistance ratio
ANOVA	analysis of variance
BDRM	blind data review meeting
CI	confidence interval
EFU	Enamel fluoride uptake
GSKCH	GlaxoSmithKline Consumer Healthcare
IRB	institutional review board
ITT	intent-to-treat
MedDRA	medical dictionary for regulatory activities
OHT	oral hard tissue
OST	oral soft tissue
PDMP	Protocol Deviation Management Plan
PP	per protocol
RER	relative erosion resistance
RLR	review listing requirement
SD	standard deviation
SE	standard error
SMHR	surface micro hardness recovery
SOC	System Organ Class
TEAE	treatment emergent adverse event
TLF	tables, listings and figures

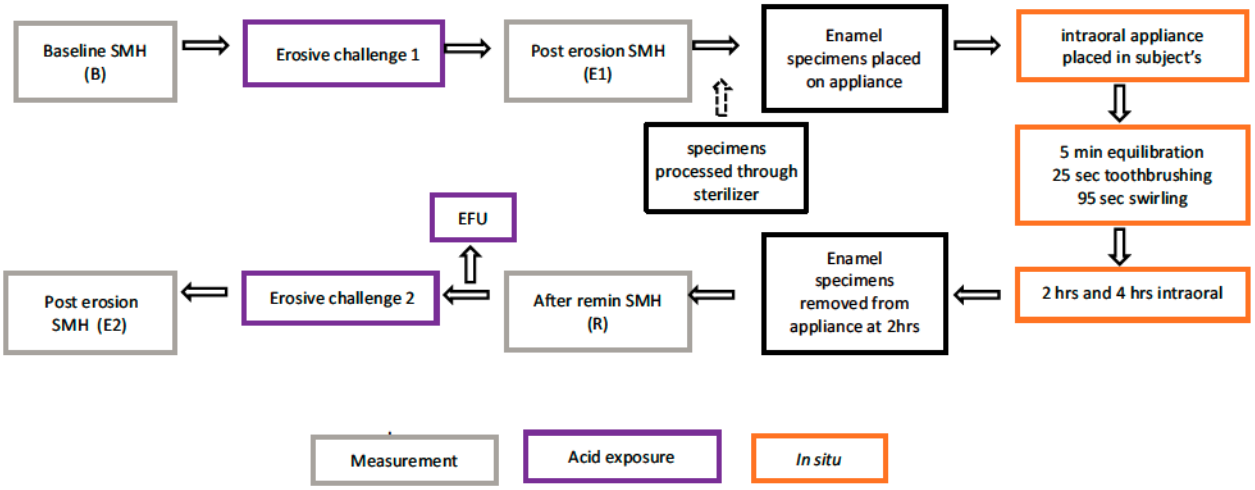
The purpose of this Statistical Reporting and Analysis Plan is to describe the planned analyses and outputs to be included in the Clinical Study Report for Protocol 208166.

1 Summary of Key Protocol Information

The aim of this study is to investigate the performance of an experimental dentifrice formulation in promoting enamel remineralization and inhibiting post-treatment enamel demineralization in an *in situ* erosion model, in comparison with a fluoride-free placebo and with a marketed competitor dentifrice product.

1.1 Study Design

This will be a randomized, controlled, single center, single- blind (to the dental examiner and specimen analysts), 3 period, 3 treatment, cross-over, *in situ* design which consists of placing pre-eroded bovine enamel specimens intra orally using a palatal appliance and testing the remineralizing performance of the experimental, comparator and placebo dentifrices 2 and 4 hours post treatment application, based on surface micro hardness measurements. This study will be carried out in healthy adults with a maxillary dental arch suitable for the retention of the palatal appliance.
There will be 4 visits, 1 screening visit to assess subject eligibility and 3 treatment visits to assess product efficacy, where the treatment product will be dispensed and used under the supervision of a suitably trained study site personnel. Prior to each treatment visit, there will be a washout period of a minimum of 3 days. During this period subjects will use their own dentifrice for at least one day, and a fluoride free dentifrice (provided) for two days prior to the next scheduled visit (including in the morning of the scheduled visit) to minimize any carry-over effects of the fluoride toothpaste.
The overall study design sequence of events is sketched in the figure below:



1.2 Study Objectives

Objectives	Endpoints
Primary Objective	
To investigate the efficacy of an experimental dentifrice containing 1150 ppm fluoride and5% KNO_3 to enhance remineralization of enamel relative to a fluoride free placebo dentifrice.	%SMHR after 4 hours intraoral phase following a single exposure.
Secondary Objectives	
Efficacy	
To investigate the efficacy of an experimental dentifrice containing 1150 ppm fluoride and 5% KNO_3 to inhibit demineralization of enamel relative to a fluoride free placebo dentifrice.	%RER after 4 hours intraoral phase following a single exposure.
To investigate the efficacy of an experimental dentifrice containing 1150 ppm fluoride and 5% KNO_3 to promote fluoride uptake in ename relative to a fluoride free placebo dentifrice.	EFU after 4 hours intraoral phase following a a single exposure.
To investigate the efficacy of an experimental dentifrice containing 1150 ppm fluoride and 5% KNO_3 to enhance remineralization, to inhibit demineralization and to promote fluoride uptake in enamel relative to a benchmark comparator containing 1100 ppm fluoride (Crest Pro Health).	%SMHR, %RER and EFU after 4 hours intraoral phase following a single exposure.
Safety	
To evaluate the oral tolerance of an experimental dentifrice containing 1150 ppm fluoride and 5% KNO_3 following a single brushing event.	Proportion of treatment emergent oral adverse events post 4 hours intraoral exposure.
Exploratory Objectives	**Exploratory Endpoints**
To make all paired comparisons of the efficacy of an experimental dentifrice containing 1150 ppm fluoride and 5% KNO_3 after 2 hours of intraoral exposure to enhance remineralization of enamel, to inhibit demineralization of enamel and to	%SMHR, %RER and EFU after 2 hours intraoral phase following a single exposure.

Objectives	Endpoints
promote fluoride uptake in enamel.	
To characterize the efficacy of the experimental dentifrice containing 1150 ppm fluoride and 5% KNO_3; the fluoride free placebo; and the benchmark comparator containing 1100 ppm (Crest Pro Health) after 2 and 4 hours of intraoral exposure on resistance to acid challenge.	Summary statistic table of ARR after 2 and 4 hours intraoral phase.

Abbreviations: SMHR: Surface micro hardness recovery, RER: Relative erosion resistance, EFU: Enamel fluoride uptake, ARR: Acid resistance ratio

1.3 Treatments

This is a single blind study, with the examiner and specimen analyst being blind to the treatment each subject received. Given that it is almost impossible to ensure identical appearance, taste and packaging for the dentifrices evaluated in this study, the level of blindness for this study is described as 'examiner blind' only. All study products (experimental, comparator and placebo dentifrices) will be over-wrapped in white vinyl to maintain the study blind as much as possible.
Subjects will be assigned to study product sequence in accordance with the randomization schedule generated by Inventiv Health under the supervision of the Biostatistics Department, GlaxoSmithKline Consumer Health (GSK CH), prior to the start of the study, using a validated program. Subjects will be randomized in a Williams square design balanced for first period carryover.

The details of the study treatments is outlined in below table

	Test Product	Comparator Product	Placebo Product
Product Name	Experimental dentifrice containing 0.254% w/w sodium fluoride (1150 ppm fluoride) and 5% KNO_3; plus 0.25% PVM/MA copolymer and 2.5% sodium lactate	Crest ProHealth Sensitivity & Enamel Shield containing 0.454% w/w stannous fluoride (1100 ppm fluoride)	Fluoride free placebo containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate

Product Formulation Code (MFC)	CCI [redacted]	Commercially available (US marketed)	CCI [redacted]
Dose	1.5 g	1.5 g	1.5 g
Route of Administration	Oral	Oral	Oral
Dosing Instructions	Subjects will apply a full ribbon of the allocated product and brush the buccal surfaces of their natural teeth for 25 timed seconds and then swish the resulting toothpaste slurry around the mouth, without further brushing, for a timed period of 95 seconds. After expectorating the slurry, the subjects will gently rinse their mouths with 15 mL of tap water for 10 seconds before expectorating again		

1.4 Sample Size Calculation

A sufficient number of healthy subjects will be screened so that up to 66 subjects are randomized to participate in the study to ensure 60 evaluable subjects complete the entire study. CCI [redacted]

A sample size of 60 subjects will be large enough to also detect a difference of 7.4 in RER with 80% power.

A sufficient number of healthy adult subjects will be selected from the Oral Health Research Institue's IRB approved database of previous research studies or from persons expressing interest in participating in research, and screened for participation.

2 Planned Analyses

2.1 Interim Analysis

No interim analysis is planned.

2.2 Final Analyses

The final planned primary analyses will be performed after the completion of the following sequential steps:

1. All subjects have completed the study as defined in the protocol.
2. All required database cleaning activities have been completed and database has been locked.
3. All criteria for unblinding the randomization codes have been met and the randomization codes have been distributed.

3 Considerations for data analyses and Data Handling Conventions

3.1 Baseline Definition

For Efficacy analyses:

Subject level baseline is defined as the latest assessment with a non-missing value before the first erosive challenge.

Period level baseline is defined as the latest assessment with a non-missing value the first erosive challenge for a given period.

Unless otherwise stated, if baseline data is missing no derivation will be performed and will be set to missing.

3.2 Subgroups/Stratifications

No stratification or subgrouping is planned for this study.

3.3 Centers Pools

This is single centre study, therefore pooling of centers is not applicable.

3.4 Timepoints and Visit Windows

The study schedule should be followed as per protocol. Deviations from the study schedule with respect to visit timings and the amount of time the appliance was worn at each visit will be reviewed and significant deviations in timings classified as protocol deviations potentially affecting efficacy assessment. A time window non-compliance listing will be produced for blinded data review.

4 Data Analysis

Data analysis will be performed by inVentiv Health Clinical. The statistical analysis software used will be SAS version 9.4 (Studio) or higher.

Prior to database closure a blind data review meeting (BDRM) will be conducted in which various aspects of the trial will be discussed and agreed.

Unless otherwise described, all listings will be produced for all randomized subjects.

4.1 Populations for Analysis

4.1.1 Subject Disposition

Screen failures are defined as subjects who consent to participate in the study but are never subsequently randomized. A summary of the number of subjects screened and the number of screen failures will be provided. Percentage calculation for screen failures will based on all screened subjects.

Subject disposition will be summarized as the number and percentage of subjects who complete the study, with the number who discontinue, broken down by reason for discontinuation. The percentages are based on the total number of subjects randomized. The table will also summarise the number and percent of subjects assigned to each analysis population (defined in Section 4.1.3). The summary will be presented by treatment group and overall (Table 14.1.1). In addition summary will be presented by sequence group, period and overall (Table 14.1.2).

Subject disposition including the subject status (completer, Yes/No), critical demographic data (age, sex and race) will be listed for randomized subjects (Listing 16.2.1.1) and non-randomized subjects (Listing 16.2.1.2) separately.

4.1.2 Protocol Deviations

Protocol deviations will be tracked by the study team throughout the conduct of the study. All deviations will be reviewed prior to unblinding and closure of the database to ensure all important deviations are captured and categorised.

The following will be taken into consideration when determing the protocol deviations with the potential to affect primay efficacy assessment.

- Deviation from the inclusion/exclusion criteria
- Use of prohibited medication before or during the study which is deemed to affect the assessment of efficacy.
- Significant non-compliance of product use.
- Significant non-compliance with the study schedule e.g., with regards to durations that appliances are worn.
- Significant deviation from planned time of an evaluation.
- Treatment not received in defined order.
- Any other reason identified which may affect the assessment of efficacy.

Major deviations deemed to affect primary efficacy will be identified between the Biostatistician and Clinical Research Director or designee, before breaking the study blind and will be documented in the Population Definition Document. These will be excluded from the Per-Protocol (PP) analysis.

Minor deviations will be identified as those not classified as major deviations.

More details on protocol deviations can be found in the Protocol Deviation Management Plan (PDMP) of this study.

The number and percentage of subjects with any major protocol deviations and with each type of major protocol deviations will be presented by treatment (Table 14.1.3) and listed (Listing 16.2.2.1). Any minor protocol deviations will be listed similarly (Listing 16.2.2.2).

4.1.3 Analysis Populations

Following analysis populations are defined.

Population	Definition / Criteria	Analyses Evaluated
All Screened Subjects	All subjects who are screened	Disposition
Randomized	All subjects who are randomized and may or may not receive the study treatment.	Protocol deviations
Safety	Safety population includes all subjects who are randomized and receive at least one dose of study treatment during the study. Safety population summaries will be presented by treatment received.	Safety analysis
Intent-to-Treat (ITT)	The primary population for efficacy assessment will be the (ITT) population, defined as all subjects who are randomized, receive the study treatment at least once and provide at least one post-baseline (post treatment) assessment of primary efficacy. All ITT population summaries and analyses will be presented by treatment randomized.	Efficacy analysis
PP	The PP population is defined as all subjects in the ITT population who have at least one assessment of the primary endpoint efficacy considered unaffected by protocol violations.	Primary efficacy analysis (%SMHR) only

Efficacy analysis on PP population will be performed only if there is more than 10% difference in the overall number of subjects between PP and ITT populations.

A decision on whether a PP analysis will be performed will be made prior to study unblinding. Subjects excluded from any of the analysis populations will be listed (Listing 16.2.3.1).

4.2 Subject Demographics and Other Baseline Characteristics

4.2.1 Demographic Characteristics

Demographic and baseline characteristics summaries will be produced for the Safety Population (Table 14.1.4.1). ITT Population (Table 14.1.4.2), and PP Population (Table 14.1.4.3) (if PP analysis is performed).

Categorical demographic variables include sex, ethnicity and race, will be summarized by the number and percentage of subjects in each treatment group. The continuous demographic variable age (in years) and will be summarized by the mean, standard deviation (SD), median, minimum and maximum values. All summaries will be presented by overall.

All demographic information will be listed for randomized subjects (Listing 16.2.4.1).

4.2.2 General Medical History

Medical history and current medical conditions for all randomized subjects will be listed (Listing 16.2.4.2) with start date and end date or ongoing at the first application of study drug.

4.3 Treatments (Study Drug, Rescue Medication, other Concomitant Therapies, Compliance)

Treatment compliance will also be listed for the blinded data review and specified in the review listing requirement (RLR) document.

4.3.1 Study Product Compliance and Exposure

Subjects will complete diary cards during the 2 days of washout period prior to the treatment visit. Study product compliance will be listed (Listing 16.2.5.3).

4.3.2 Prior and Concomitant Medication

Prior medications are defined as those stopped before the first administration of study drug.

Any medication that has started prior to first dose of study drug and is still continuing is termed as concomitant medication.

Concomitant medication is also defined as any medication taken between the date of first dose of study drug and the date of last dose of study drug.

In this crossover trial, medications will be assigned to the treatment group based on the treatment being received at that date. Medications with a date time between treatments periods will be assigned to the treatment received in the previous period. Medications with a date after last treatment or the end of the study will be assigned to the treatment taken in the last period.

There will be no imputation of unknown dates. However if the start date is unknown, then it will be assumed to concomitant (all treatment periods) unless the partial start date or stop date indicates differently.

Prior and concomitant medications and siginificant non-drug therapies will be listed by subject, with preferred term, indication, dose, dose form, frequency, route, start date, end date or ongoing and start day relative to first dose of study drug (Listing 16.2.5.1 and Listing 16.2.5.2).

4.4 Analysis of Efficacy

4.4.1 Primary Efficacy Endpoint

4.4.1.1 Primary Efficacy Endpoint Definition

The primary efficacy endpoint is %SMHR after 4 hours of remineralization.

Definition of primary variable: % SMH recovery = [(E1-R)/(E1-B)] * 100

B = indentation length (µm) of sound enamel at baseline
E1 = indentation length (µm) after first erosive challenge
R = indentation length (µm) after *in situ* remineralization

Per subject %SMHR will be determined from the %SMHR calculated for each specimen using five indentations measurements per specimen, averaged across the four specimens at 4 hours. Therefore, a single observation per treatment for each subject will be used in the statistical analyses. If a subject is missing an enamel specimen, the mean will be computed over the available enamel specimens.

4.4.1.2 Statistical Hypothesis, Model, and Method of Analysis

The primary comparison of this study is the 1150 ppm fluoride experimental dentifrice versus the fluoride free placebo (0 ppmF) in %SMHR at 4 hours and must be statistically significant to meet the success criteria.

The extent of remineralization will be calculated as the % recovery in SMH (%SMHR), which is calculated from the enamel indentation length at baseline, after the first erosive challenge and after the *in situ* remineralization phase after 4 hrs of intraoral phase.

Statistical testing of all endpoints in this study will be conducted at a two-sided significance level of 0.05. As a primary objective has been defined prior to analysis, there will be no adjustment for multiple comparisons. The null and alternative hypotheses are

- H_0: there is no difference between treatment groups;
- H_1: there is a difference between treatment groups.

The analysis of variance (ANOVA) will be used to analyze the treatment difference. The ANOVA model will include fixed factors for study period and treatment, and a random effect for subject. The baseline SMH and first demineralization level will not be included in the model as covariates as the samples will be preselected so that each sample has a measurement of 43 +/-3 µm at baseline (B) and 10-20 µm greater than the baseline after the first erosive challenge (E1).

Summary statistics including mean, standard deviation (SD), standard error (SE), median, min, max will be provided on the analysis population used for statistical analysis (Table 14.2.1.1) by treatment group.

Adjusted means of two treatments and treatment difference will be provided together with 95% confidence interval (CI) and p-values (Table 14.2.1.1) by treatment group.

The assumption of residual normality and variance homogeneity in ANOVA analysis will be investigated through residual plots. If violated, a nonparametric method (paired Wilcoxon Sign Rank test) will be performed. If the violation is caused by extreme values, a sensitivity analysis will be conducted by removing the extreme values and same analysis will be repeated without those extreme values. If nonparametric test is performed and the inferences on treatment comparisons are similar to that of ANOVA, both sets of results will be reported and the emphasis will be made on the ANOVA results. Otherwise, nonparametric results will be used to draw conclusions.

A Bar Chart (Figure 14.2.1.5) with Error Bars (±SD) will be created.

4.4.1.3 Supportive Analyses

If there are more than 10% differences in the overall number of subjects between PP and ITT populations, a PP analysis will be performed for primary efficacy variable. This analysis would be considered as supportive analysis (Table 14.2.1.3).

A summary table (Table 14.2.1.4) for derived specimens by timepoint and treatment groups will be provided.

4.4.2 Secondary Efficacy Variables

Secondary efficacy variables of the study are defined in section 4.5.

4.4.3 Handling of Missing Values/Censoring/Discontinuations

Missing data will not be replaced or imputed. Dropouts will be included in analyses up to the point of discontinuation.

4.5 Analysis of Secondary Objectives

The treatment difference, SE and 95% CI will be presented for all of the comparisons however the p-values for these secondary comparisons will only be presented if the primary comparison is statistically significant.

Same model and analysis methods of primary efficacy endpoint will be conducted for all secondary efficacy endpoints.

4.5.1.1 Percent Relative Erosion Resistance (RER) after 4 Hours

The %RER is calculated based on the indentation length at baseline, after the first and the second erosive challenge after 4 hours.

% Relative Erosion Resistance = [(E1-E2) / (E1-B)] * 100
B= Indentation length (µm) of sound enamel at baseline
E1= Indentation length (µm) after first erosive challenge
E2= Indentation length (µm) after second erosive challenge

Per subject % RER will be determined from the % RER calculated for each specimen using five indentations measurements per specimen, averaged across the four specimens at 4 hours. Therefore, a single observation per treatment for each subject will be used in the statistical analyses. If a subject is missing an enamel specimen, the mean will be computed over the available enamel specimens.

Summary statistics including mean, SD, SE, median, min, max will be provided on the analysis population used for statistical analysis (Table 14.2.2.1) by treatment group. Adjusted means of two treatments and treatment difference will be provided together with 95% confidence interval (CI) and p-values (Table 14.2.2.1) by treatment group. As a primary objective has been defined prior to analysis, there will be no adjustment for multiple comparisons.

A Bar Chart (Figure 14.2.2.3) with Error Bars (±SD) will be created.

4.5.1.2 Enamuel Fluoride Uptake (EFU) after 4 Hours

EFU is assessed by the microdrill enamel biopsy, and is determined after 4 hours *in situ* remineralization period but before the second extra-oral erosive challenge. This measurement will provide with micrograms of fluoride per square centimeter (µg F/cm^2).

Per subject EFU score will be calculated as follows: microdrill samples from each enamel specimen will be pooled and a value for fluoride content per enamel specimen determined. These values will be averaged across the four enamel specimens for each subject and time point to produce the subject-wise mean enamel fluoride uptake.

Summary statistics including mean, standard deviation (SD), standard error (SE), median, min, max will be provided on the analysis population used for statistical analysis (Table 14.2.3.1) by treatment group. Adjusted means of two treatments and treatment difference will

be provided together with 95% CI and p-values (Table 14.2.3.1) by treatment group. As a primary objective has been defined prior to analysis, there will be no adjustment for multiple comparisons.

A Bar Chart (Figure 14.2.3.3) with Error Bars (±SD) will be created.

4.5.2 Exploratory Efficacy Variables

Exploratory variables of the study are listed below. Unless not stated otherwise same model and analysis methods will be conducted as for the secondary endpoints.

4.5.2.1 Percent Surface Microhardness Recovery after 2 Hours

The extent of remineralization will be calculated as the % recovery in SMH, which is calculated from the enamel indentation length at baseline, after the first erosive challenge and after the *in situ* remineralization phase after 2 hours of intraoral phase.

Summary statistics including mean, SD, SE, median, min, max will be provided on the analysis population used for statistical analysis (Table 14.2.1.2) by treatment group. Adjusted means of two treatments and treatment difference will be provided together with 95% CI and p-values (Table 14.2.1.2) by treatment group. As a primary objective has been defined prior to analysis, there will be no adjustment for multiple comparisons.

A Bar Chart (Figure 14.2.1.5) with Error Bars (±SD) will be created.

4.5.2.2 Percent Relative Erosion Resistance after 2 Hours

This end point aims to test whether the formulations prevents enamel demineralization after the 2 hours intra oral remineralization phase as per a second erosion challenge. The %RER is calculated based on the indentation length at baseline, after the first and the second erosive challenge after 2 hours.

Summary statistics including mean, SD, SE, median, min, max will be provided on the analysis population used for statistical analysis (Table 14.2.2.2) by treatment group. Adjusted means of two treatments and treatment difference will be provided together with 95% CI and p-values (Table 14.2.2.2) by treatment group. As a primary objective has been defined prior to analysis, there will be no adjustment for multiple comparisons.

A Bar Chart (Figure 14.2.2.3) with Error Bars (±SD) will be created.

4.5.2.3 Enamuel Fluoride Uptake (EFU) after 2 Hours

EFU is assessed by the microdrill enamel biopsy, and is determined after 2 hours *in situ* remineralization period but before the second extra-oral erosive challenge. This measurement will provide with micrograms of fluoride per square centimeter (µg F/cm^2).

Summary statistics including mean, SD, SE, median, min, max will be provided on the analysis population used for statistical analysis (Table 14.2.3.2) by treatment group. Adjusted means of two treatments and treatment difference will be provided together with 95% CI and

p-values (Table 14.2.3.2) by treatment group. As a primary objective has been defined prior to analysis, there will be no adjustment for multiple comparisons.

A Bar Chart (Figure 14.2.3.3) with Error Bars (±SD) will be created.

4.5.2.4 Acid Resistance Ratio (ARR)

The ARR measures acid resistance of the treated enamel after 2 and 4 hours intraoral phase. It is calculated based on the indentation length after the second erosive challenge and the *in situ* remineralization phase, and after the first erosive challenge and baseline.

The ARR will be calculated as follows: ARR = 1- [(E2-R) / (E1-B)]

B= Indentation length (µm) of sound enamel at baseline
E1= Indentation length (µm) after first erosive challenge
E2= Indentation length (µm) after second erosive challenge
R = indentation length (µm) after in situ remineralization

Only summary statistics including mean, SD, SE, median, min, max will be provided by randomized treatment group (Table 14.2.4.1, Table 14.2.4.2) for 4 hours and 2 hours respectively.

A Bar Chart (Figure 14.2.4.3) with Error Bars (±SD) will be created.

4.6 Analysis of Safety

4.6.1 Adverse Events and Serious Adverse Events

All summaries of safety will be performed using the safety population and will be analyzed based on treatment actually received. No formal statistical testing will be performed on summary comparisons related to safety related measurements.

All AEs will be coded using the medical dictionary for regulatory activities (MedDRA). AEs will be classified by system organ class (SOC) and by preferred term (PT). In addition, prior to database lock all AEs will be reviewed by the Clinical Research Director (or designee) and categorized as either oral or non-oral. Safety will be assessed based on any oral AEs (this includes those that are identified as treatment emergent oral soft tissue (OST) abnormalities and spontaneously reported oral AEs). Any new or worsening OST condition that occurs after the OST examinations at Screening will be recorded as an AE.

In this crossover trial, events will be assigned to the treatment group based on the treatment being received at the onset of the event. TEAEs with an onset date time between treatments perods will be assigned the treatment received in the previous period. TEAEs with an onset after last treatment or the end of the study will be assigned to the treatment taken in the last period. If an emergent AE continues to another treatment period and worsens, the AE will be

considered emergent in both the period in which it started and also the period in which it worsened.

AEs will be summarized using descriptive statistics (frequency tables) by treatment group. Summary tables will indicate both the number of events and the number (percent) of subjects involved. Summaries of AEs will also include TEAEs unless otherwise noted. TEAEs are defined as new AEs that occur on or after the date/time of the first supervised use of the randomized treatment (or events aggravated in severity following treatment). Events with an onset date/time prior to first use of a treatment will be considered as non-treatment emergent.

The following summary tables and listings will be presented by treatment group.

- Table of Treatment emergent AEs by SOC and PT (Table 14.3.1.1)
- Table of Treatment emergent AEs by Oral/Non-Oral and PT (Table 14.3.1.2)
- Table of treatment emergent treatment related AEs by SOC and Preferred Term (Table 14.3.1.3).
- Table of treatment emergent treatment related AEs by Oral/Non-Oral and Preferred Term (Table 14.3.1.4).
- Table of treatment emergent AEs by intensity and Preferred Term. (Table 14.3.1.5).
- Listing of all AEs (including all subjects: Listing 16.2.7.1 for all randomized subjects; Listing 16.2.7.2 for non-randomized subjects).
- Listing of death (Listing 14.3.2.1).
- Listing of serious AEs (Listing 14.3.2.2) (if there are more than 5 treatment emergent serious AEs (SAEs) a table (Table 14.3.1.6) will be produced instead by SOC and PT).
- Listing of treatment emergent AEs leading to withdrawal (Listing 14.3.2.3).
- Listing of treatment emergent AEs classified as oral (Listing 14.3.2.4).
- Listing of non-fatal serious treatment emergent AEs (Listing 14.3.2.5) (only produced if there are more than 5 SAEs).

In the event that there is nothing to report a null listing will be produced.

4.6.2 Other Safety Variables

A listing (Listing 16.2.7.3) for incidents will be produced. A table (Table 14.4.1.1) for OST will be produced for changes in abnormality pre- and post treatment. In addition a listing (Listing 16.2.9.2) for oral hard tissue (OHT) and OST (Listing 16.2.9.1) will be displayed.

4.7 Analysis of Other Variables

Not applicable.

5 Changes to the Protocol Defined Statistical Analysis Plan

There are no changes to the protocol-planned statistical analyses.

Top-line Summary:

For the top-line report selected outputs will be produced as documented in the attached worksheet excel file.

Appendix 1: Subgroups

Not Applicable

Appendix 2: Center pools in multicenter studies

Not Applicable

Appendix 3: Major Protocol Deviations

Protocol deviations will be tracked by the study team throughout the conduct of the study. More details on protocol deviations can be found in the Protocol Deviation Management Plan (PDMP) of this study.

All deviations will be reviewed prior to study unblinding and closure of the database. Details will be given in the populations' definitions document.

Attachment 1: List of Data Display

Worksheet in
208166_RAP Final v1

Appendix 4: Templates for Tables, Figures & Listings

The following provides detail of the treatment labels to be used on the table, figure and listings and and general footnotes.

The treatment labels will be specified as follows:

Test Product
Comparator Product
Placebo Product

If there are no data to display generate a null table or listing.

Add following footnote to all TFLs:

Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

Protocol No. 208166 Program Run Date:xxxx

Table 14.1.1
Subject Disposition by Treatment Group Across Study Treatment Periods
All Screened Subjects

All Screened Subjects (N=xxx)

	Test Product n (%)	Comparator Product n (%)	Placebo Product n (%)	Overall n (%)
TOTAL SUBJECTS SCREENED				xxx
SUBJECTS NOT RANDOMIZED				xxx
DID NOT MEET STUDY CRITERIA				xxx (xx.x)
ADVERSE EVENT				xxx (xx.x)
LOST TO FOLLOW UP				xxx (xx.x)
PROTOCOL VIOLATION				xxx (xx.x)
WITHDRAWAL OF CONSENT				xxx (xx.x)
OTHER				xxx (xx.x)
SUBJECTS RANDOMIZED	xxx	xxx	xxx	xxx
COMPLETED STUDY	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
DID NOT COMPLETE STUDY	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
DID NOT MEET STUDY CRITERIA	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
ADVERSE EVENT	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
LOST TO FOLLOW-UP	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
PROTOCOL VIOLATION	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
WITHDRAWAL OF CONSENT	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
OTHER	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
SAFETY POPULATION				xxx (xx.x)
ITT POPULATION				xxx (xx.x)
PP POPULATION				xxx (xx.x)

For categories under 'Subjects Not Randomized' percentages will be calculated using the number of 'All Screened Subjects' as the denominator. Percentages under the 'Subjects Randomized' categories will be computed using number of subjects randomized as the denominator.
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Table 14.1.2
Subject Disposition by Sequence Group and Period
All Screened Subjects

All Screened Subjects (N=xxx)

	Treatment Sequence						
	A/B/C	A/C/B	B/A/C	B/C/A	C/A/B	C/B/A	OVERALL
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
TOTAL SUBJECTS SCREENED							XX
SUBJECTS NOT RANDOMIZED:							XX
DID NOT MEET STUDY CRITERIA							XX
ETC.							..
SUBJECTS RANDOMIZED	XX	XX	XX	XX	XX	XX	XX
PERIOD X:							
STARTED PERIOD:	XX	XX	XX	XX	XX	XX	XX
COMPLETED	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
DID NOT COMPLETE:	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
DID NOT MEET STUDY CRITERIA	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
ETC.	..	..	..	..	..	..	..
SAFETY POPULATION	XX	XX	XX	XX	XX	XX	XX
ITT POPULATION	XX	XX	XX	XX	XX	XX	XX
PP POPULATION	XX	XX	XX	XX	XX	XX	XX

A=Test Product; B=Comparator Product; C=Placebo Product
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Table 14.1.3
Incidence of Major Protocol Deviations
All Randomized Subjects

Randomized Population (N=xxx)

	A/B/C		A/C/B		B/A/C		B/C/A		C/A/B		C/B/A		Overall	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
SUBJECTS WITH AT LEAST ONE MAJOR PROTOCOL VIOLATION	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)
MAJOR PROTOCOL VIOLATIONS NOT LEADING TO EXCLUSION FROM PP	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)
VIOLATION REASON 1	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)
MAJOR PROTOCOL VIOLATIONS LEADING TO EXCLUSION FROM PP	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)
All VISITS														
VIOLATION REASON 1	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)
WEEK Y	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)
VIOLATION REASON 1	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)	xxx	(xx.x)

A=Test Product; B=Comparator Product; C=Placebo Product
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Table 14.1.4.1
Demographics Characteristics
Safety Population

Safety Population (N=xxx)	Overall N (%)
SEX n (%)	
Male	xx (xx.x)
Female	xx (xx.x)
RACE n (%)	
African American/African Heritage	xx (xx.x)
American Indian or Alaskan Native	xx (xx.x)
Asian - Central/South Asian Heritage	xx (xx.x)
Asian - East Asian Heritage	xx (xx.x)
Asian - Japanese Heritage	xx (xx.x)
Asian - South East Asian Heritage	xx (xx.x)
Native Hawaiian or Other Pacific Islander	xx (xx.x)
White - Arabic/North African Heritage	xx (xx.x)
White - White/Caucasian/European Heritage	xx (xx.x)
ETHNICITY n (%)	
Hispanic or Latino	xx (xx.x)
Not Hispanic or Latino	xx (xx.x)
AGE (YEARS)	
N	xx
MEAN	xx.x
SD	xx.xx
MEDIAN	xx.x
MINIMUM	xx
MAXIMUM	xx

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Table 14.2.1.1
Statistical Analysis of Percent Surface Microhardness Recovery at 4 Hours by Treatment Group
ITT Population

Intent-to-Treat Population (N=XX)

	Test Product (N=XX)	Comparator Product (N=XX)	Placebo Product (N=XX)
n	xx	xx	xx
MEAN	x.xx	x.xx	x.xx
SD	x.xxx	x.xxx	x.xxx
SE	x.xxx	x.xxx	x.xxx
MEDIAN	x.xx	x.xx	x.xx
MINIMUM	X.xx	x.xx	x.xx
MAXIMUM	X.xx	x.xx	x.xx
ADJUSTED MEAN [1]	xx.xx	xx.xx	xx.xx
STANDAR ERROR	x.xxx	x.xxx	x.xxx

COMPARISON BETWEEN TREATMENTS	DIFFERENCE [1,2]	95% CI [1]	P-VALUE [1]
TEST PRODUCT VS PLACEBO PRODUCT	x.xx	(xx.xx, xx.xx)	x.xxxx
TEST PRODUCT VS COMPARATOR PRODUCT	x.xx	xx.xx, xx.xx)	x.xxxx

[1] From ANOVA with fixed factors for study period and treatment, and a random effect for subject.
[2] Difference is first-named treatment minus second-named treatment such that a positive difference favors the first named treatment.
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Table 14.2.1.4
Summary Table of Indents Measures by Timepoint and Treatment Group
ITT Population

Intent-to-Treat Population (N=XX)

Timepoint	Treatment	N	Indentation length of sound enamel at baseline (B) (μm) Mean	SE	Indentation length after first Erosive Challenge (E1) (μm) Mean	SE	Indentation length after second Erosive Challenge (E2) (μm) Mean	SE	*Indentation length after in situ* Remineralization (R) (μm) Mean	SE
4 Hours	Test Product	XX	xx.xx	x.xxx	xx.xx	x.xxx	xx.xx	x.xxx	xx.xx	x.xxx
	Comparator Product	XX	xx.xx	x.xxx	xx.xx	x.xxx	xx.xx	x.xxx	xx.xx	x.xxx
	Placebo Product	XX	xx.xx	x.xxx	xx.xx	x.xxx	xx.xx	x.xxx	xx.xx	x.xxx
2 Hours	Test Product	XX	xx.xx	x.xxx	xx.xx	x.xxx	xx.xx	x.xxx	xx.xx	x.xxx
	Comparator Product	XX	xx.xx	x.xxx	xx.xx	x.xxx	xx.xx	x.xxx	xx.xx	x.xxx
	Placebo Product	XX	xx.xx	x.xxx	xx.xx	x.xxx	xx.xx	x.xxx	xx.xx	x.xxx

Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Figure 14.2.1.5
Bar Chart with Error Bars (+/- SD) for % Surface Microhardness Recovery
ITT Population

Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Programming Note: Please adapt this figure with study specfic informations and title specifications. Please include 2 hour and 4 hour in same figure.

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Table 14.2.4.1
Summary Statistics of Acid Resistance Ratio (ARR) at 4 Hours by Treatment Group
ITT Population

Intent-to-Treat Population (N=XX)

	Test Product (N=XX)	Comparator Product (N=XX)	Placebo Product (N=XX)
n	xx	xx	xx
MEAN	x.xx	x.xx	x.xx
SD	x.xxx	x.xxx	x.xxx
SE	x.xxx	x.xxx	x.xxx
MEDIAN	x.xx	x.xx	x.xx
MINIMUM	x.xx	x.xx	x.xx
MAXIMUM	x.xx	x.xx	x.xx

Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Table 14.3.1.1
Treatment Emergent Adverse Event by System Organ Class and Preferred Term
Safety Population

Safety Population (N=xx)

SOC Preferred Term	Test Product (N=XX)		Comparator Product (N=XX)		Placebo Product (N=XX)		Overall (N=XXX)	
	n (%)	nAE	n (%)	nAE	n (%)	nAE	n (%)	nAE
NUMBER OF SUBJECTS WITH AT LEAST ONE AE	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
NUMBER OF SUBJECTS WITH NO AE	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
ERYTHEMA	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
DERMATITIS	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
GASTROINTESTINAL SYSTEM	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
ABDOMINAL PAIN	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
DRY MOUTH	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
VOMITTING	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
Etc.								

n (%) = Number (percent) of subjects nAE = Number of adverse events. SOC=System organ class
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Table 14.3.1.2
Treatment Emergent Adverse Event by Oral/Non-Oral and Preferred Term
Safety Population

Safety Population (N=xx)

	Test Product (N=XX)			Comparator Product (N=XX)			Placebo Product (N=XX)			Overall (N=XXX)		
Preferred Term	n	(%)	nAE	n	(%)	nAE	n	(%)	nAE	n	(%)	nAE
NUMBER OF SUBJECTS WITH AT LEAST ONE TEAE	xx	(xx.x)	xx	xx	(xx.x)	xx	xx	(xx.x)	xx	xx	(xx.x)	xx
NUMBER OF SUBJECTS WITH NO TEAE	xx	(xx.x)		xx	(xx.x)		xx	(xx.x)		xx	(xx.x)	
ORAL	xx	(xx.x)	xx	xx	(xx.x)	xx	xx	(xx.x)	xx	xx	(xx.x)	xx
SENSITIVITY OF TEETH	xx	(xx.x)	xx	xx	(xx.x)	xx	xx	(xx.x)	xx	xx	(xx.x)	xx
ORAL MUCOSAL EXOLIATION	xx	(xx.x)	xx	xx	(xx.x)	xx	xx	(xx.x)	xx	xx	(xx.x)	xx
NON ORAL	xx	(xx.x)	xx	xx	(xx.x)	xx	xx	(xx.x)	xx	xx	(xx.x)	xx
BRONCHITIS	xx	(xx.x)	xx	xx	(xx.x)	xx	xx	(xx.x)	xx	xx	(xx.x)	xx
COUGH	xx	(xx.x)	xx	xx	(xx.x)	xx	xx	(xx.x)	xx	xx	(xx.x)	xx

n (%) = Number (percent) of subjects nAE = Number of adverse events.
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Table 14.3.1.5
Treatment Emergent Adverse Events by Intensity and Preferred Term
Safety Population

Study Population: Safety Population

Preferred Term	Intensity	Test Product N=XXX n	(%)	[AEs]	Comparator Product N=XXX n	(%)	[AEs]	Placebo Product N=XXX n	(%)	[AEs]	Overall (N=XXX) n	(%)	[AEs]
Preferred Term #1	MILD	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]
	MODERATE	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]
	SEVERE	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]
Preferred Term #2	MILD	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]
	MODERATE	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]
	SEVERE	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]
Preferred Term #3	MILD	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]
	MODERATE	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]
	SEVERE	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]	XXX	(XX.X)	[XXX]

n (%) = Number (percent) of subjects nAE = Number of adverse events.
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Table 14.4.1.1
Summary of Oral Soft Tissue - Changes from Pre-treatment to Post-treatment
Safety Population

Safety Population (N=xx)

			Post-Treatment (4 hours)		
			Normal	Abnormal	Not Examined
Treatment	AREA	Pre-Treatment	n (%)	n (%)	n (%)
Test Product					
	Labial Mucosa	Normal	XX (XX.X)	XX (XX.X)	XX (XX.X)
		Abnormal	XX (XX.X)	XX (XX.X)	XX (XX.X)
		Not Examined	XX (XX.X)	XX (XX.X)	XX (XX.X)
	Buccal Mucosa	Normal	XX (XX.X)	XX (XX.X)	XX (XX.X)
		Abnormal	XX (XX.X)	XX (XX.X)	XX (XX.X)
		Not Examined	XX (XX.X)	XX (XX.X)	XX (XX.X)
	[other]	Normal	XX (XX.X)	XX (XX.X)	XX (XX.X)
		Abnormal	XX (XX.X)	XX (XX.X)	XX (XX.X)
		Not Examined	XX (XX.X)	XX (XX.X)	XX (XX.X)
Comparator Product					
Placebo Product					

Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Programmer Note: please add all different areas for all treatments.

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Listing 16.1.7.1
Randomization Details
All Randomized Subjects

Subject Number	Age/Sex/ Race [1]	Randomization Number	Treatment Sequence [2]	Randomization Date
PPD				

[1] Age in years; Sex: F=Female, M=Male; Race: A1=African American/African Heritage, A2=American Indian Or Alaskan Native, A3=Asian-Central/South Asian Heritage, A4=Asian-East Asian Heritage, A5=Asian-Japanese Heritage, A6=Asian-South East Asian Heritage, N=Native Hawaiian Or Other Pacific Islander, W1=White-Arabic/North African Heritage, W2=White-White/Caucasian/European Heritage, MT=Multiple.
[2] A=Test Product; B=Comparator Product; C=Placebo Product
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Programmer Note: correct seed number an block size to be added after unblinding in a footnote

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Listing 16.2.1.1
Subject Disposition
All Randomized Subjects

Treatment Sequence: XXXXXXXXXX

Subject Number	Age/Sex/ Race [1]	Screening Date	Period	Treatment Start Date and Time	Date of Completion or Withdrawal	Period of Withdrawal	Completed (Yes/No)	Primary Reason for Withdrawal	Further Details [2]
PPD									

[1] Age in years; Sex: F=Female, M=Male; Race: A1=African American/African Heritage, A2=American Indian Or Alaskan Native, A3=Asian-Central/South Asian Heritage, A4=Asian-East Asian Heritage, A5=Asian-Japanese Heritage, A6=Asian-South East Asian Heritage, N=Native Hawaiian Or Other Pacific Islander, W1=White-Arabic/North African Heritage, W2=White-White/Caucasian/European Heritage, MT=Multiple.

[2] Further details of reasons for withdrawal.

A=Test Product; B=Comparator Product; C=Placebo Product
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Listing 16.2.1.2
Subject Disposition
Non-Randomized Subjects

Subject Number	Age/Sex/ Race [1]	Screening Date	Reason for Screen Failure	Further Details [2]
PPD				

[1] Age in years; Sex: F=Female, M=Male; Race: A1=African American/African Heritage, A2=American Indian Or Alaskan Native, A3=Asian-Central/South Asian Heritage, A4=Asian-East Asian Heritage, A5=Asian-Japanese Heritage, A6=Asian-South East Asian Heritage, N=Native Hawaiian Or Other Pacific Islander, W1=White-Arabic/North African Heritage, W2=White-White/Caucasian/European Heritage, MT=Multiple.
[2] Further details of reasons for screen failure.

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Listing 16.2.2.1
Important and Major Protocol Deviations
All Randomized Subjects

Treatment Sequence: XXXXXXXXXX

Subject Number	Age/Sex/Race [1]	Period	Deviation Sequence	Date of Deviation	Deviation Type	Deviation Description
XXXXXX	XX/F/A1		1	28JUN201	XXXXXX	XXXXXX

[1] Age in years; Sex: F=Female, M=Male; Race: A1=African American/African Heritage, A2=American Indian Or Alaskan Native, A3=Asian-Central/South Asian Heritage, A4=Asian-East Asian Heritage, A5=Asian-Japanese Heritage, A6=Asian-South East Asian Heritage, N=Native Hawaiian Or Other Pacific Islander, W1=White-Arabic/North African Heritage, W2=White-White/Caucasian/European Heritage, MT=Multiple.
A=Test Product; B=Comparator Product; C=Placebo Product
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Programming Note: Listing 16.2.2.1 lists only those identified in population definition document to be excluded from PP population.

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Listing 16.2.2.2
Minor Protocol Deviations
Randomized Population

Treatment Sequence: XXXXXXXXXX

Subject Number	Age/Sex/ Race [1]	Period	Deviation Sequence	Protocol Deviation
PPD				xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

[1] Age in years; Sex: F=Female, M=Male; Race: A1=African American/African Heritage, A2=American Indian Or Alaskan Native, A3=Asian-Central/South Asian Heritage, A4=Asian-East Asian Heritage, A5=Asian-Japanese Heritage, A6=Asian-South East Asian Heritage, N=Native Hawaiian Or Other Pacific Islander, W1=White-Arabic/North African Heritage, W2=White-White/Caucasian/European Heritage, MT=Multiple.
A=Test Product; B=Comparator Product; C=Placebo Product
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Protocol No. 208166 Program Run Date:xxxx

Listing 16.2.3.1
Exclusions from Analysis Populations
All Randomized Subjects

Treatment Sequence: XXXXXXXXXX

Subject Number	Age/Sex/ Race [1]	Randomized	Safety	ITT	Per Protocol
PPD					

[1] Age in years; Sex: F=Female, M=Male; Race: A1=African American/African Heritage, A2=American Indian Or Alaskan Native, A3=Asian-Central/South Asian Heritage, A4=Asian-East Asian Heritage, A5=Asian-Japanese Heritage, A6=Asian-South East Asian Heritage, N=Native Hawaiian Or Other Pacific Islander, W1=White-Arabic/North African Heritage, W2=White-White/Caucasian/European Heritage, MT=Multiple.
A=Test Product; B=Comparator Product; C=Placebo Product
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Protocol No. 208166 Program Run Date:xxxx

Listing 16.2.4.1
Demographic Characteristics
All Randomized Subjects

Treatment Sequence: XXXXXXXXXX

Subject Number	Sex	Race	Age (years)	Ethnicity
PPD				

A=Test Product; B=Comparator Product; C=Placebo Product
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Protocol No. 208166 Program Run Date:xxxx

Listing 16.2.4.2
Medical History and Current Medical Conditions
All Randomized Subjects

Treatment Sequence: XXXXXXXXXX

Subject Number	Age/Sex/ Race [1]	Any Medical History?	Medical Condition	Start Date	Ongoing?	End Date
PPD						

[1] Age in years; Sex: F=Female, M=Male; Race: A1=African American/African Heritage, A2=American Indian Or Alaskan Native, A3=Asian-Central/South Asian Heritage, A4=Asian-East Asian Heritage, A5=Asian-Japanese Heritage, A6=Asian-South East Asian Heritage, N=Native Hawaiian Or Other Pacific Islander, W1=White-Arabic/North African Heritage, W2=White-White/Caucasian/European Heritage, MT=Multiple.

A=Test Product; B=Comparator Product; C=Placebo Product
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Protocol No. 208166 Program Run Date:xxxx

Listing 16.2.5.1
Prior Medications and Significant Non-Drug Therapies Prior to Treatment
All Randomized Subjects

Treatment Sequence: XXXXXXXXXX

Subject Number	Age/Sex/ Race [1]	Treatment (GSK Drug Synonym)	Reason for Medication	Route of Administration	Dose per Administration	Frequency	Start Date (Study Day [2])	End Date/ Ongoing
PPD								

[1] Age in years; Sex: F=Female, M=Male; Race: A1=African American/African Heritage, A2=American Indian Or Alaskan Native, A3=Asian-Central/South Asian Heritage, A4=Asian-East Asian Heritage, A5=Asian-Japanese Heritage, A6=Asian-South East Asian Heritage, N=Native Hawaiian Or Other Pacific Islander, W1=White-Arabic/North African Heritage, W2=White-White/Caucasian/European Heritage, MT=Multiple.
[2] Study day relative to the date of first dose of treatment.

A=Test Product; B=Comparator Product; C=Placebo Product
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Listing 16.2.5.2
Concomitant Medications and Significant Non-Drug Therapies During Treatment
All Randomized Subjects

Treatment Sequence: XXXXXXXXXX

Subject Number	Age/Sex/ Race [1]	Treatment (GSK Drug Synonym)	Medication assigned Period	Reason for Medication	Route of Administration	Dose per Administration	Frequency	Start Date (Study Day [2])	End Date/ Ongoing
PPD									

[1] Age in years; Sex: F=Female, M=Male; Race: A1=African American/African Heritage, A2=American Indian Or Alaskan Native, A3=Asian-Central/South Asian Heritage, A4=Asian-East Asian Heritage, A5=Asian-Japanese Heritage, A6=Asian-South East Asian Heritage, N=Native Hawaiian Or Other Pacific Islander, W1=White-Arabic/North African Heritage, W2=White-White/Caucasian/European Heritage, MT=Multiple.
A=Test Product; B=Comparator Product; C=Placebo Product
[2] Study day relative to the date of first dose of treatment.
A=Test Product; B=Comparator Product; C=Placebo Product
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Programmer Note: Subject will be listed by treatment groups. Same subjects could be listed on different treatment groups

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Listing 16.2.5.3
Study Product Compliance
All Randomized Subjects

Subject Number	Age/Sex/ Race [1]	Treatment Sequence	Period	Subject Compliance to use of washout period (Yes/No)	Number of missed product uses since the last visit	Number of additional product uses since the last visit
PPD						

[1] Age in years; Sex: F=Female, M=Male; Race: A1=African American/African Heritage, A2=American Indian Or Alaskan Native, A3=Asian-Central/South Asian Heritage, A4=Asian-East Asian Heritage, A5=Asian-Japanese Heritage, A6=Asian-South East Asian Heritage, N=Native Hawaiian Or Other Pacific Islander, W1=White-Arabic/North African Heritage, W2=White-White/Caucasian/European Heritage, MT=Multiple.
A=Test Product; B=Comparator Product; C=Placebo Product
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Listing 16.2.6.1
Surface Microhardness Recovery
All Randomized Subjects

Treatment Sequence: XXXXXXXXXX

Subject Number	Age/Sex/ Race [1]	Timepoint	Specimen Information	Period	Treatment	Measurement	Indentation length of sound enamel at baseline (B) (µm)	Indentation length after first Erosive Challenge (E1) (µm)	*Indentation length after in situ* Remineralization (R) (µm)	% SMHR
PPD										

[1] Age in years; Sex: F=Female, M=Male; Race: A1=African American/African Heritage, A2=American Indian Or Alaskan Native, A3=Asian-Central/South Asian Heritage, A4=Asian-East Asian Heritage, A5=Asian-Japanese Heritage, A6=Asian-South East Asian Heritage, N=Native Hawaiian Or Other Pacific Islander, W1=White-Arabic/North African Heritage, W2=White-White/Caucasian/European Heritage, MT=Multiple.
Each value is calculated as the average of five indentations measurements per specimen, averaged across the four specimens for 2hours or 4hours.
A=Test Product; B=Comparator Product; C=Placebo Product
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Programmer Note: Please add all "other" information and timepoints for each subject in chronological order. For each subject we will have four specimen informations (XXX1 to XXX4) per subject and period. Overall endpoint value to be calculated as mean of averages per period.

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Listing 16.2.6.2
Relative Erosion Resistance
All Randomized Subjects

Treatment Sequence: XXXXXXXXXX

Subject Number	Age/Sex/ [1]	Race	Timepoint	Specimen Information	Period	Treatment	Measurement	Sound Enamel at Baseline (µm)	First Erosive Challenge (µm)	Indentation length after second Erosive Challenge (E2) (µm)	% RER
PPD											

[1] Age in years; Sex: F=Female, M=Male; Race: A1=African American/African Heritage, A2=American Indian Or Alaskan Native, A3=Asian-Central/South Asian Heritage, A4=Asian-East Asian Heritage, A5=Asian-Japanese Heritage, A6=Asian-South East Asian Heritage, N=Native Hawaiian Or Other Pacific Islander, W1=White-Arabic/North African Heritage, W2=White-White/Caucasian/European Heritage, MT=Multiple.
Each value is calculated as the average of five indentations measurements per specimen, averaged across the four specimens for 2hours or 4hours.

A=Test Product; B=Comparator Product; C=Placebo Product
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

PPD

Programmer Note: Please add all "other" information and timepoints for each subject in chronological order. For each subject we will have four specimen informations (XXX1 to XXX4) per subject and period. Overall endpoint value to be calculated as mean of averages per period.

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Listing 16.2.6.3
Enamel Fluoride Uptake
All Randomized Subjects

Treatment Sequence: XXXXXXXXXX

Subject Number	Age/Sex/ [1]	Race	Timepoint	Period	Treatment	Specimen Information 1	Specimen Information 2	Specimen Information 3	Specimen Information 4	Enamel Fluoride Uptake
PPD										

[1] Age in years; Sex: F=Female, M=Male; Race: A1=African American/African Heritage, A2=American Indian Or Alaskan Native, A3=Asian-Central/South Asian Heritage, A4=Asian-East Asian Heritage, A5=Asian-Japanese Heritage, A6=Asian-South East Asian Heritage, N=Native Hawaiian Or Other Pacific Islander, W1=White-Arabic/North African Heritage, W2=White-White/Caucasian/European Heritage, MT=Multiple.
A=Test Product; B=Comparator Product; C=Placebo Product
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Listing 16.2.6.4
Acid Resistance Ratio
All Randomized Subjects

Treatment Sequence: XXXXXXXXXX

Subject Number	Age/Sex/ Race [1]	Timepoint	Specimen Information	Period	Treatment	Measurement	Sound Enamel at Baseline (µm)	First Erosive Challenge (µm)	Second Erosive Challenge (µm)	*In situ* Remineralization (µm)	Acid Resistance Ratio
PPD											

[1] Age in years; Sex: F=Female, M=Male; Race: A1=African American/African Heritage, A2=American Indian Or Alaskan Native, A3=Asian-Central/South Asian Heritage, A4=Asian-East Asian Heritage, A5=Asian-Japanese Heritage, A6=Asian-South East Asian Heritage, N=Native Hawaiian Or Other Pacific Islander, W1=White-Arabic/North African Heritage, W2=White-White/Caucasian/European Heritage, MT=Multiple.
Each value is calculated as the average of five indentations measurements per specimen, averaged across the four specimens for 2hours or 4hours.

A=Test Product; B=Comparator Product; C=Placebo Product
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Programmer Note: Please add all "other" information and timepoints for each subject in chronological order. For each subject we will have four specimen informations (XXX1 to XXX4) per subject and period. Overall endpoint value to be calculated as mean of averages per period.

Protocol No. 208166 Program Run Date:xxxx

Listing 16.2.7.1
Adverse Events
All Randomized Subjects

Treatment Sequence: XXXXXXXXXX

Subject Number	Age/Sex/ Race [1]	Adverse Event (Preferred Term) [System of Organ Class]	Start Date (Study Day) [2]	Start Time	End Date	End Time	AE assigned Period	Frequency/ Intensity[3]	Related to Study Product?	Action Taken re Study Product	Outcome	Serious?	With-drew? [4]
PPD													

@@ Adverse events with verbatim text ending in this are classified as Oral AEs.
[1] Age in years; Sex: F=Female, M=Male; Race: A1=African American/African Heritage, A2=American Indian Or Alaskan Native, A3=Asian-Central/South Asian Heritage, A4=Asian-East Asian Heritage, A5=Asian-Japanese Heritage, A6=Asian-South East Asian Heritage, N=Native Hawaiian Or Other Pacific Islander, W1=White-Arabic/North African Heritage, W2=White-White/Caucasian/European Heritage, MT=Multiple.
[2] Study day is the day relative to start of treatment, Day 1 being the day of first treatment. Period day is the day relative to the start of treatment being received in that period
[3] INT = Intermittent and SGLE = Single. [4] Did subject withdraw from study as a result of this adverse event?
A=Test Product; B=Comparator Product; C=Placebo Product
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Protocol No. 208166 Program Run Date:xxxx

Listing 16.2.7.2
Adverse Events
Non-Randomized Subjects

Subject Number	Age/Sex/ Race [1]	Adverse Event (Preferred Term) [System of Organ Class]	Start Date	Start Time	End Date	End Time	Frequency/ Intensity[2]	Related to Study Product?	Action Taken re Study Product	Outcome	Serious?	With-drew? [3]
PPD												

@@ Adverse events with verbatim text ending in this are classified as Oral AEs.
[1] Age in years; Sex: F=Female, M=Male; Race: A1=African American/African Heritage, A2=American Indian Or Alaskan Native, A3=Asian-Central/South Asian Heritage, A4=Asian-East Asian Heritage, A5=Asian-Japanese Heritage, A6=Asian-South East Asian Heritage, N=Native Hawaiian Or Other Pacific Islander, W1=White-Arabic/North African Heritage, W2=White-White/Caucasian/European Heritage, MT=Multiple.
[2] INT = Intermittent and SGLE = Single.
[3] Did subject withdraw from study as a result of this adverse event?

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Protocol No. 208166 Program Run Date:xxxx

Listing 16.2.7.3
Listing of Incidents
All Randomized Subjects

Treatment Sequence: XXXXXXXXXX

Subject Number	Age/Sex/Race[1]	Treatment	Period	Date of the Incident	Incident
PPD					

[1] Age in years; Sex: F=Female, M=Male; Race: A1=African American/African Heritage, A2=American Indian Or Alaskan Native, A3=Asian-Central/South Asian Heritage, A4=Asian-East Asian Heritage, A5=Asian-Japanese Heritage, A6=Asian-South East Asian Heritage, N=Native Hawaiian Or Other Pacific Islander, W1=White-Arabic/North African Heritage, W2=White-White/Caucasian/European Heritage, MT=Multiple.
A=Test Product; B=Comparator Product; C=Placebo Product
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Protocol No. 208166 Program Run Date:xxxx

Listing 16.2.9.1
Oral Soft Tissue Examination
All Randomized Subjects

Treatment Sequence: XXXXXXXXXX

Subject Number	Age/Sex/ Race [1]	Visit	Timepoint	Date of Assessment	Time of Assessment	Area	Abnormality	Details for not examined
PPD								

[1] Age in years; Sex: F=Female, M=Male; Race: A1=African American/African Heritage, A2=American Indian Or Alaskan Native, A3=Asian-Central/South Asian Heritage, A4=Asian-East Asian Heritage, A5=Asian-Japanese Heritage, A6=Asian-South East Asian Heritage, N=Native Hawaiian Or Other Pacific Islander, W1=White-Arabic/North African Heritage, W2=White-White/Caucasian/European Heritage, MT=Multiple.
A=Test Product; B=Comparator Product; C=Placebo Product
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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Protocol No. 208166 Program Run Date:xxxx

Listing 16.2.9.2
Oral Hard Tissue Examination
All Randomized Subjects

Treatment Sequence: XXXXXXXXXX

Subject Number	Age/Sex/ Race [1]	Timepoint	Date of Assessment	Time of Assessment	Area	Abnormality	Details for not examined
PPD							

[1] Age in years; Sex: F=Female, M=Male; Race: A1=African American/African Heritage, A2=American Indian Or Alaskan Native, A3=Asian-Central/South Asian Heritage, A4=Asian-East Asian Heritage, A5=Asian-Japanese Heritage, A6=Asian-South East Asian Heritage, N=Native Hawaiian Or Other Pacific Islander, W1=White-Arabic/North African Heritage, W2=White-White/Caucasian/European Heritage, MT=Multiple.
A=Test Product; B=Comparator Product; C=Placebo Product
Test Product: Experimental dentifrice containing 0.254% w/w sodium fluoride (1 150 ppm fluoride) and 5% KNO_3 plus 0.25% PVM/MA copolymer and 2.5% sodium lactate; Comparator Product: Crest ProHealth Sensitivity & Enamel Shield dentifrice containing 0.454% w/w stannous fluoride (1100 ppm fluoride); Placebo Product: Fluoride free placebo dentifrice containing 5% KNO_3 (0 ppm fluoride); plus 0.25% PVM/MA copolymer and 2.5% lactate.

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