STATISTICAL REPORTING AND ANALYSIS PLAN

A METHOD DEVELOPMENT CLINICAL STUDY INVESTIGATING THE EFFICACY OF AN EXPERIMENTAL ORAL RINSE IN PROVIDING LONG TERM RELIEF FROM DENTINAL HYPERSENSITIVITY

Protocol Number: 207656

Phase: N/A

Document History

Document	Version Date	Summary of Changes (New analysis or Change in planned analysis)
Final Analysis Plan	5-Oct-2017	Not applicable (N/A)

Table of contents

Abbreviation

AE	Adverse Event
ANCOVA	Analysis Of Covariance
BDRM	Blinded Data Review Meeting
CI	Confidence Interval
DH	Dentinal Hypersensitivity
EAR	Erosion, Abrasion, Recession
eCRF	Electronic Case Report Form
GSK CH	Glaxosmithkline Consumer Healthcare
ITT	Intent-To-Treat
MedDRA	Medical Dictionary For Regulatory
N	Number Of Subjects
OHT	Oral Hard Tissue
OST	Oral Soft Tissue
PP	Per Protocol
ppm	Parts Per Million
RAP	Reporting And Analysis Plan
RLR	Review Listing Requirement
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SEs	Standard Error
SMS	Short Service Message
SOC	System Organ Class
VRS	Visual Rating Scale
w/w	Weight/Weight

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 207656.

1 Summary of Key Protocol Information

The purpose of this trial is to demonstrate the efficacy and safety of a 1.5% dipotassium oxalate monohydrate (KOX) containing oral rinse to treat the symptoms of Dentinal Hypersensitivity (DH). Efficacy will be demonstrated as a treatment difference in favour of the 1.5% KOX containing oral rinse vs. the negative control oral rinse for the primary efficacy outcome, Schiff sensitivity score at Week 8. Safety will be demonstrated through assessment of adverse events (AEs).

1.1 Study Design

Overall Design
This will be a single centre, eight week, randomized, examiner-blind, three treatment, parallel group design, stratified study in healthy subjects, with at least two sensitive teeth that meet all of the study criteria at the Screening and Baseline visits. DH will be assessed at Baseline, and after 4 and 8 weeks of twice daily treatment. At the Screening visit, subjects will give their written informed consent to participate in the study. Demography, medical history and concomitant medications will be recorded, followed by an oral examination. This will include an oral soft tissue (OST) examination, an oral hard tissue examination (OHT), dentition exclusions, assessment of erosion, abrasion, recession (EAR), gingival status, tooth mobility and subject response to a qualifying air sensitivity assessment, subject response will be recorded as a numerical value (Schiff score 2/3). Eligible subjects will be supplied with a standard fluoride dentifrice and a fluoride oral rinse to use twice daily (morning and evening) during the acclimatization period between the Screening and Baseline visits. Each product use will be recorded in the diary provided. First use of the acclimatization dentifrice and oral rinse will be carried out under supervision at the study site. At the Baseline visit (2-3 weeks after Screening), eligibility to continue will be assessed. Subjects will undergo an OST examination, followed by tooth sensitivity assessments (a tactile stimulus [Yeaple probe, maximum 20g pressure], then an evaporative air stimulus [with Schiff Sensitivity Scale and Visual Rating Score VRS]), and a review of the inclusion/exclusion criteria. Two test teeth will then be identified and eligible subjects will be randomized to treatment (stratified by maximum baseline Schiff sensitivity score of the two selected test teeth). First use of allocated study product will be carried out under supervision at the study site, after the supervised brushing subjects will be requested to measure out the dose of the oral rinse using the dosing cup provided. Subjects will continue to use their assigned study treatment twice daily (morning and evening) for the next 8 weeks, recording each brushing and rinsing occasion in the diary provided.

Subjects will return to the study site each week (Visits 3, 4, 5, 6, 7, 8, 9 and 10) over the eight week study period and asked to return their study kit so that the oral rinse bottle and its contents can be weighed to verify study compliance. Diaries will also be checked at each visit. A supervised brushing and rinse will also be conducted at each visit (except Visit 10). Following supervised product use all products will be returned to the subject. The dentifrice and oral rinse will be re-dispensed at Visit 6 (Week 4).Tooth sensitivity will be re-assessed after 4 and 8 weeks (Visits 6 and 10) of treatment, using first a tactile stimulus (Yeaple probe, maximum 80g pressure) and then an evaporative air stimulus (with Schiff Sensitivity Scale and VRS) on the two selected test teeth only. An OST examination will be completed at each of these visits, prior to the clinical assessments of sensitivity.

The study site will send twice daily (morning and evening) short message service (SMS) reminders requesting that subjects remember to conduct their timed brush and rinse in the morning and evening.

For further details please refer to Section 3.1 of the protocol.

1.2 Study Objectives

Objectives	Endpoints
Primary Objective	**Primary Endpoint**
• To evaluate and compare the clinical efficacy of a 1.5% KOX containing oral rinse for the relief of DH, as elicited by an evaporative air stimulus (with Schiff Sensitivity Scale), against a negative control oral rinse, following use as an adjunct to twice daily brushing with a standard fluoride dentifrice, after 8 weeks.	• Change from baseline in Schiff sensitivity score at 8 weeks.
Secondary Objectives	**Secondary Endpoints**
To evaluate and compare the clinical efficacy of a 1.5% KOX containing oral rinse for the relief of DH, as elicited by a tactile stimulus (Yeaple probe), against a negative control oral rinse, following use as an adjunct to twice daily brushing with a standard fluoride dentifrice, after 8 weeks.	• Change from baseline in tactile threshold (Yeaple probe) at 8 weeks.
Exploratory Objectives	**Exploratory Endpoints**

Objectives	Endpoints
• To evaluate and compare the clinical efficacy of a 1.5% KOX containing oral rinse for the relief of DH, as elicited by an evaporative air stimulus (with Schiff Sensitivity Scale), against a placebo oral rinse, following use as an adjunct to twice daily brushing with a standard fluoride dentifrice, after 8 weeks.	• Change from baseline in Schiff sensitivity score at 8 weeks.
• To evaluate and compare the clinical efficacy of a 1.5% KOX containing oral rinse for the relief of DH, as elicited by a tactile stimulus (Yeaple probe), against a placebo oral rinse, following use as an adjunct to twice daily brushing with a standard fluoride dentifrice, after 8 weeks.	• Change from baseline in tactile threshold (Yeaple probe) at 8 weeks.
• To evaluate and compare the clinical efficacy of a 1.5% KOX containing oral rinse for the relief of DH, as elicited by an evaporative air stimulus (with Schiff Sensitivity Scale), against a marketed negative control oral rinse and a placebo oral rinse, following use as an adjunct to twice daily brushing with a standard fluoride dentifrice, after 4 weeks.	• Change from baseline in Schiff sensitivity score at 4 weeks.
• To evaluate and compare the clinical efficacy of a 1.5% KOX containing oral rinse for the relief of DH, as elicited by a tactile stimulus (Yeaple probe), against a marketed negative control oral rinse and a placebo oral rinse, following use as an adjunct to twice daily brushing with a standard fluoride dentifrice, after 4 weeks.	• Change from baseline in tactile threshold (Yeaple probe) at 4 weeks.
• To evaluate and compare the clinical efficacy of a 1.5% KOX containing oral rinse for the relief of DH, as elicited an evaporative air stimulus (with VRS), against a marketed negative control oral rinse and a	• Change from baseline in Visual Rating Score (VRS) at 4 and 8 weeks.

Objectives	Endpoints
placebo oral rinse, following use as an adjunct to twice daily brushing with a standard fluoride dentifrice, after 4 and 8 weeks.	
• To evaluate and compare the clinical efficacy of a 1.5% KOX containing oral rinse for the relief of DH, as elicited by an evaporative air stimulus (with Schiff Sensitivity Scale), against the efficacy of the group obtained by combining the marketed negative control and the placebo oral rinse,following use as an adjunct to twice daily brushing with a standard fluoride dentifrice, after 4 and 8 weeks.	• Change from baseline in Schiff sensitivity score at 4 and 8 weeks.
• To evaluate and compare the clinical efficacy of a 1.5% KOX containing oral rinse for the relief of DH, as elicited by a tactile stimulus (Yeaple probe), against the efficacy of the group obtained by combining the marketed negative control and the placebo oral rinse, following use as an adjunct to twice daily brushing with a standard fluoride dentifrice, after 4 and 8 weeks.	• Change from baseline in tactile threshold (Yeaple probe) at 4 and 8 weeks.
• To evaluate and compare the clinical efficacy of a 1.5% KOX containing oral rinse for the relief of DH, as elicited an evaporative air stimulus (with VRS), against the efficacy of the group obtained by combining the marketed negative control and the placebo oral rinse, following use as an adjunct to twice daily brushing with a standard fluoride dentifrice, after 4 and 8 weeks.	• Change from baseline in VRS at 4 and 8 weeks.

1.3 Treatment

	Test Product	Negative control	Placebo Product
Product Name	Experimental oralrinse containing 1.5% KOX, 0ppm fluoride, pH 7	Oral rinse containing 0.02% w/w NaF. Colgate Total Daily Repair® (USA marketed product)	Oral rinse containing 0% KOX and 0 ppmfluoride, pH
Product Formulation Code (MFC)	CCI	Commercially Available	CCI
Route of Administration	Oral	Oral	Oral
Dosing Instructions	Rinse twice daily (morning and evening) with 10 ml of oral rinse for 60 timed seconds and expectorate. No further rinsing with water will be permitted after use of the oral rinse.	Rinse twice daily (morning andevening) with 10 mlof oral rinse for 60 timed seconds andexpectorate. Nofurther rinsing withwater will bepermitted after use ofthe oral rinse.	Rinse twice daily (morning andevening) with 10 mlof oral rinse for 60 timed seconds andexpectorate. Nofurther rinsing withwater will bepermitted after use ofthe oral rinse.

All subjects will receive the same regular fluoride dentifrice and a US marketed oral rinse during the acclimatization period to familiarise themselves with the required brushing and rinsing regimen, and standardise oral hygiene practices.

Subjects will apply a full brush head of the standard fluoride dentifrice, brush for one timed minute (in their usual manner) and expectorate; rinse with 10 ml of tap water for 5 seconds and expectorate; and then rinse with 10 ml of their randomly assigned oral rinse for 60 timed seconds and expectorate. No further rinsing with water will be permitted after use of the oral rinse, and subjects will be asked to refrain from eating or drinking within 30 minutes of using the oral rinse. The dosage regimen of twice daily treatment (morning and evening) will be the same for all subjects.

1.4 Sample Size Calculation

A sufficient number of healthy subjects will be screened to randomise at least 100 subjects (approximately 50 to the experimental treatment, 25 to the negative control and 25 to placebo) to ensure 80 evaluable subjects complete the entire study. This will ensure approximately 40 evaluable subjects for the test treatment and 20 each for the negative control treatment and placebo.

With this 2:1:1 distribution of the subjects in the treatment arms, the study has less than 50% power to detect a mean treatment difference of 0.36 in the Schiff sensitivity score using a two-sided t-test of significance level 0.05 for the experimental product against the negative control. The standard deviation used in this calculation is 0.8; this estimate is obtained from the GSKCH study 204763. When the experimental treatment group is compared with the combined group comprising of the negative control group and the placebo group using the two-sided t-test with the same estimates of mean difference, significance level and standard deviation, the study will have 51.1% power.

The magnitude of the treatment difference is more important and is expected to be in favour of the experimental mouthwash.

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 all endpoints the baseline value will be the latest Day-0 pre-dose assessment with a non-missing value.

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

3.2 Subgroups/Stratifications

Eligible subjects will be stratified according to their maximum baseline Schiff sensitivity score of the two selected teeth. The stratification factor will give rise to two strata.

Stratum 1: Subjects with maximum baseline Schiff sensitivity score of 2 for the two selected test teeth.

Stratum 2: Subjects with the maximum baseline Schiff sensitivity score of 3 for the two selected test teeth.

Efficacy variables will be analyzed accounting for strata.

Subgroups are not defined for this trial.

3.3 Centers Pools

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

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 will be reviewed on a case-by-case basis to determine whether the data should be excluded from the Per-Protocol (PP) analysis (Section 4.1.2).

4 Data Analysis

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

Prior to database closure a Blinded Data Review Meeting (BDRM) will be conducted in which various aspects of the trial will be discussed and agreed.

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

4.1 Populations for Analysis

4.1.1 Subject Disposition

Screen failures will be defined as subjects who do not satisfy all of the inclusion/exclusion criteria. A summary will be provided of the number of subjects screened and the number of screen failures with reasons why subjects were not randomized (Table 14.1.1). Percentages will be based on the total number of subjects randomized.

Subject disposition will also be summarized as the number and percentage of subjects who complete the study, with the number who discontinue broken down by reason for discontinuation (Table 14.1.1). 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 and overall.

Subject disposition including the subject status (completer, Yes/No), critical demographic data (age, sex, race and ethnicity), the duration of treatment before discontinuation and the specific reason for discontinuation, will be listed by treatment group for randomized subjects (Listing 16.2.1.1) and non-randomized subjects (Listing 16.2.1.2) separately.

4.1.2 Protocol Deviations

Important major protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, patient management or patient assessment) will be summarized and listed.

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

Major deviations of the protocol procedures identified as liable to influence the efficacy outcome may include, but will not be necessarily limited to, the following:

- Violations of inclusion or exclusion criteria
- Prior / concomitant medications
- Ineligible teeth
- Treatment non-compliance
- Not receiving randomized treatment
- Visit outside the planned schedule

Further deviations liable to influence the efficacy outcome will be given in the Review Listing Requirement (RLR) document where major deviations will be identified at the blinded data review meeting. 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 14.1.2) and listed in Listing 16.2.2.1. Any minor protocol deviations will be listed similarly (Listing 16.2.2.2).

4.1.3 Analysis Populations

Five analysis populations are defined.

Population	Definition / Criteria	Analyses Evaluated
All Screened Subjects	• All subjects who enter the study and sign the informed consent form. This population includes screen failures as well as those that are randomized	• Disposition, AE listing

Population	Definition / Criteria	Analyses Evaluated
Randomized	• All subjects who are randomized and may or may not receive the application of the study products. • Any subject who receives a treatment Randomization number will be considered to have been randomized	• Protocol violations
Safety	• Comprise of all randomized subjects who receive at least one dose of study treatment. • This population will be based on the treatment the subject actually received.	• Safety
Intent-To-Treat	• Comprise of all randomized subjects who receive at least one dose of study treatment and have at least one post-baseline efficacy evaluation. • This population will be based on the treatment to which the subject was randomized.	• Efficacy
Per-Protocol	• The 'Per-Protocol' (PP) population will include all subjects in the ITT population who have no protocol deviations deemed to affect efficacy.	• Efficacy

The primary population for assessment of efficacy will be the ITT population. A PP analysis will be performed on the primary and secondary efficacy variable if more than 10% of the subjects in the ITT population are excluded from the PP population.

The numbers of subjects included in each of the populations, and the number excluded from each population broken down by the reason for exclusion will be presented (Table 14.1.2). 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

Descriptive statistics (number of subjects, mean, standard deviation, median, minimum and maximum for continuous variables, and frequency and percentage for categorical variables) will be presented for demographic data by treatment group and overall. These data include age, gender, race, ethnicity and Schiff stratification categories and will be presented for the Safety (Table 14.1.4.1), ITT (Table 14.1.4.2) and if required the PP populations (Table 14.1.4.3).

Demographic information will be listed (Listing 16.2.4.1) for all randomized subjects.

4.2.2 General Medical History

Medical history data will be listed (Listing 16.2.4.2) with start date and end date or ongoing at the start of study drug. A data listing will also be produced for evaluation of protocol violations at the blinded data review stage.

4.3 Study Product Compliance and Use of Other Therapy

Supervised brushing/rinsing non complince (subject number, date of visit and time of the supervised procedure and reason why the supervised brushing was not performed according to the protocol) will be listed for the blinded data review and specified in the RLR document.

4.3.1 Study Product Compliance and Exposure

Brushing/rinsing compliance (using study product twice daily) will be listed for the blinded data review and specified in the RLR document.

4.3.2 Prior and Concomitant Medication

Prior medications will be listed by subject, with, indication, dose, dose form, frequency, route, start date and end date (Listing 16.2.5.1). Prior medications are defined as those stopped before the first administration of the study products.Concomitant medications will be listed similarly (Listing 16.2.5.2). Concomitant medications are defined as those ongoing or started on or after the first administration of the study products.

4.3.3 Other Therapy/Rescue Medication

Not Applicable.

4.4 Analysis of Efficacy

4.4.1 Primary Efficacy Endpoint

4.4.1.1 Primary Efficacy Endpoint Definition

The change from baseline in Schiff sensitivity score at Week 8 is the primary efficacy endpoint.

The subjects Schiff sensitivity score will be derived as the mean of the two test teeth at each visit assessed and the change from baseline will be derived from this mean Schiff score. For for post-baseline observations, the average will be calculated only across teeth that have both a valid baseline and a valid postbaseline assessment.

Summary statistics of the observed mean Schiff sensitivity scores and changes from basline will be presented by treatment at Baseline, Week 4 and Week 8 (Table 14.2.1.1.1).

To visually inspect the treatment effect on Schiff sensitivity scores, a plot across time, with the raw means together with standard error (SEs) bars will be produced. The plot will display a different symbol line for each treatment group (Figure 14.2.1).

4.4.1.2 Statistical Hypothesis, Model, and Method of Analysis

The primary analysis is a comparison of the mean change from baseline Schiff sensitivity score between Test Product and Negative Control at Week 8.

The null hypothesis for the primary endpoint is that the mean change from baseline in Schiff sensitivity score is equal between the two products.

H0: $\mu_1 = \mu_2$

The alternative hypothesis is that the mean change from baseline in Schiff sensitivity score is not equal between the two products.

H1: $\mu_1 \neq \mu_2$

The change from baseline in Schiff sensitivity score at Week 8 will be analyzed using ANCOVA with treatment as factor and mean baseline Schiff sensitivity score as covariate. Note that since the baseline Schiff sensitivity score will be included as a covariate, the baseline Schiff stratification value will not be included in the model. Adjusted means of all treatments and their SEs, P-value and 95% confidence interval (CIs) will be presented on the ITT population (Table 14.2.1.1.2). Treatment differences of the treatment comparisons will also be provided together with P-values and 95% CIs.

The assumption of normality and homogeneity of variance in the ANCOVA model will be investigated and if violated, data transformations will be investigated. If suitable transformations cannot be found, non-parametric Van Elteren tests will be performed adjusting for the maximum baseline Schiff sensitivity scores and results will be compared with the ANCOVA results. If the inferences from the two analyses are similar then both sets of results will be reported and emphasis will be made on the ANCOVA results. In case of discrepancies between p-values of ANCOVA and Van Elteren analysis, inferences will be drawn on the non-parametric analysis.

To visually inspect the treatment effect on Schiff sensitivity scores, a plot across time (Baseline, Week 4 and Week 8) will be displayed with raw means and SE bars. The plot will display a different symbol line for each treatment group (Figure 14.2.1).

4.4.1.3 Supportive Analyses

The change from baseline in Schiff sensitivity score to post-treatment (Week 4 and 8) will be summarized and analyzed as detailed for the primary endpoint. Analysis assumptions will be investigated as detailed for the primary efficacy analysis.

The analysis will be conducted for:

- Test Product versus Placebo Product at Week 4 and 8
- Test Product versus Negative Control at Week 4

Similar analyses for a Combined Control group (Negative Control and Placebo) will also be performed for the changes from baseline in Schiff sensitivity score to Weeks 4 and 8 using the same ANCOVA model mentioned above for the analysis of the primary efficacy variable.

The adjusted mean for each treatment, and the difference between the pairs of treatments together with their corresponding 95% CIs and the P-values for treatment comparisons, will be provided (Table 14.2.1.1.2).

Test Product versus Combined Control group will be obtained by using contrast at Week 4 and 8. Below comparison will be tested:

- Test product versus Combined Control group at Week 4 and 8

4.4.2 Secondary Efficacy Variables

Secondary efficacy variables are defined in section 4.5

4.4.3 Handling of Missing Values/Censoring/Discontinuations

Missing data will not be replaced or imputed. Subjects who withdraw from the study prematurely will be included in the statistical analyses up to the point of discontinuation.

4.5 Analysis of Secondary Objectives

4.5.1 Efficacy (Secondary)

The change from baseline in tactile threshold at Week 8

The change from baseline in tactile threshold at Week 8 is the secondary efficacy endpoint.

The null hypothesis for the secondary endpoint is that the mean change from baseline in tactile threshold is equal between the two products.

$\mathbf{H_0}$: $\mu_1 = \mu_2$

The alternative hypothesis is that the mean change from baseline in tactile threshold score is not equal between the two products.

$\mathbf{H_1}$: $\mu_1 \neq \mu_2$

The primary treatment comparison of this secondary efficacy variable is:

Test Product versus Negative Product at Week 8.

All other treatment comparisons based on secondary efficacy variable are part of the exploratory objectives.

The subjects tactile threshold will be derived as the mean of the two test teeth at each visit assessed and the change from baseline will be derived from this mean tactile threshold. If tactile threshold for test teeth reported greater than 80g for post baseline assessment then in that case it will be consider as 90g.

Summary statistics of the observed mean tactile threshold scores and changes from baseline will be presented by treatment at Baseline, Week 4 and Week 8 (Table 14.2.2.1).

The change from baseline in tactile threshold at Week 8 will be calculated as the subject level mean change from baseline (on the two test teeth) and analyzed at Week 8 using ANCOVA with treatment and baseline Schiff stratification value as factors and baseline tactile threshold included as a covariate. Adjusted means of all treatments and their SEs, P-value and 95% CIs

will be presented . Treatment differences of all pairs of treatments will be provided together with P-values and 95% CIs (Table 14.2.2.2).

To visually inspect the treatment effect on tactile threshold scores, a plot across time, with the raw means together with SE bars will be produced. The plot will display a different symbol line for each treatment group (Figure 14.2.2).

The assumption of normality and homogeneity of variance in the ANCOVA model will be investigated and if violated, data transformations will be investigated. If suitable transformations cannot be found, non-parametric Van Elteren tests will be performed adjusting for the maximum baseline Schiff sensitivity scores and results will be compared with the ANCOVA results. If the inferences from the two analyses are similar then both sets of results will be reported and emphasis will be made on the ANCOVA results. In case of discrepancies between p-values of ANCOVA and van Elteren analysis, inferences will be drawn on the non-parametric analysis.

4.5.1.1 Exploratory Analysis of Secondary Efficacy Variable

The change from baseline in tactile threshold score to post-treatment (Week 4 and 8) will be summarized and analyzed as detailed for the secondary endpoint. Analysis assumptions will be investigated as detailed for the secondary efficacy analysis (Section 4.5.1).

The analysis will be conducted for:

- Test Product versus Placebo at Week 4 and 8
- Test Product versus Negative Control at Week 4

Analyses for the Combined Control group (Placebo and Negative Control) will also be done for the changes from baseline in tactile threshold score to Weeks 4 and 8 using the same ANCOVA model mentioned above for the analysis of the secondary efficacy variable.

The adjusted mean for each treatment, and the difference between the pairs of treatments together with their corresponding 95% CIs and the P-values for treatment comparisons, will be provided (Table 14.2.2.2).

Test Product versus Combined Control group will be obtained by using contrast at Week 4 and 8.

4.5.2 Pharmacokinetic (Secondary)

Not Applicable

4.6 Analysis of Exploratory Objective

Exploratory analysis based on the primary and secondary efficacy variable (change from baseline in Schiff sensitivity score and change from baseline in tactile threshold) are discussed in the section above.

Raw values of the visual rating score (VRS) (averaged over the two test teeth) at Week 4 and Week 8 together with changes from baseline will be summarized by treatment at each study time point (Table 14.2.3.1). To visually inspect the treatment effect on Schiff sensitivity

scores, a plot across time, with the raw means together with SEs bars will be produced. The plot will display a different symbol line for each treatment group (Figure 14.2.3).

The change from baseline in VRS will be calculated as the subject level mean change from baseline (on the two test teeth) and analyzed separately at Week 4 and 8 using ANCOVA with treatment and baseline Schiff stratification value as factors and baseline VRS score included as a covariate. Adjusted means of all treatments and their SE, P-value and 95% CIs will be presented. Treatment differences of all pairs of treatments will be provided together with P-values and 95% CIs (Table 14.2.3.2).

The assumption of normality and homogeneity of variance in the ANCOVA model will be investigated and if violated, data transformations will be investigated. If suitable transformations cannot be found, non-parametric Van Elteren tests will be performed adjusting for the maximum baseline Schiff sensitivity scores and results will be compared with the ANCOVA results. If the inferences from the two analyses are similar then both sets of results will be reported and emphasis will be made on the ANCOVA results. In case of discrepancies between p-values of ANCOVA and van Elteren analysis, inferences will be drawn on the non-parametric analysis.

Analyses for the Combined Control group will also be performed on the change from baseline in VRS to Weeks 4 and 8 using the same ANCOVA model mentioned above .

The adjusted mean for each treatment, and the difference between the pairs of treatments together with their corresponding 95% CIs and the p-values for treatment comparisons, will be provided (Table 14.2.3.2).

Test Product versus Combined Control group will be obtained by using contrast at Week 4 and 8.

All data for each efficacy measure will be presented for each subject at Baseline, Week 4 and Week 8 (Listing 16.2.6.1, Listing 16.2.6.2 and Listing 16.2.6.3).

4.7 Analysis of Safety

4.7.1 Adverse Events and Serious Adverse Events

All safety data will be reported for the Safety population as per actual treatment received. The safety profile of the study treatments will be assessed with respect to AEs. OST abnormalities are included as AEs if they appear or worsen after the initial assessment.

All AEs will be reviewed by the Clinical Research Director or Designee prior to database freeze and will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). During this review stage, AEs will be further categorized as oral or non-oral.

AEs will be regarded as treatment-emergent if they occur on or after the start date and time of the first treatment usage (as determined by start date and time from the EXPOSURE/dispensing panel; if this date is missing a suitable alternative will be used eg date of randomization). All other AEs prior to this will be considered non-treatment emergent.

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

- Table of treatment emergent AEs by system organ class (SOC) and Preferred Term (Table 14.3.1.1)
- Table of treatment emergent AEs by Oral/Non-Oral and Preferred Term (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)
- Listing of all AEs (Listing 16.2.7.1 for all randomized subjects; Listing 16.2.7.2 for non-randomized subjects)
- Listing of deaths (Listing 14.3.2.1)
- Listing of non-fatal SAEs (Listing 14.3.2.2)
- Listing of treatment emergent AEs leading to study or drug withdrawal (Listing 14.3.2.3)
- Listing of treatment emergent AEs classified as oral (Listing 14.3.2.4)

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

4.7.2 Other Safety Variables

All incidents (refer to section 7.6 of the protocol for further details on incidents) captured in the study will be listed in Listing 16.2.7.3. In the event that there is nothing to report, a null listing will be produced.

4.8 Analysis of Other Variables

Not applicable.

5 Changes to the Protocol Defined Statistical Analysis Plan

Changes from the originally planned statistical analysis specified in the protocol are outlined in below table:

Protocol	Reporting & Analysis Plan	
Statistical Analysis section	**Statistical Analysis Plan**	**Rationale for Changes**
9.2.1. Definition of Analysis Populations A Per protocol (PP) analysis will be performed on the primary variable only if more than 10% of the subjects in the ITT population have protocol deviations deemed to affect efficacy	• A PP analysis will be performed on the primary and secondary efficacy variable if more than 10% of the subjects in the ITT population are excluded from the PP population	• Endpoints based on the secondary efficacy variable (tactile threshold) are important in this trial.

6 Top-line Summary

The outputs required for the topline is summary is documented in the attached worksheet excel file.

Attachment 1: List of Data Displays

Study 207656_List of Outputs_01Oct2017.

Appendix 1: Templates for Tables, Figures & Listings

This is a guideline which will give the guidance of treatment labels that will be used for the table header and in the figures, listings and in the footnotes.

Note to programmer:

1) *The treatment labels for the column heading will be as follow:*

- *Test Product*
- *Negative Control*
- *Placebo*

2) *Use following footnotes in all the TLFs:*

Test Product: Oral Rinse (1.5% KOX, 0ppm F, pH 7) - MFC04905
Negative Control: Oral Rinse 2 (0.02% w/w NaF) Colgate Total Daily Repair
Placebo: Oral Rinse (0% KOX, 0ppm F, pH 7) – MFC04939

3) *Check actual races captured in eCRF to adjust the race name and abbreviations.*

Protocol 207656 Program Run Date:xxxx

Table 14.1.1
Subject Disposition
All Subjects

Study Population: All Screened Subjects (N=xxx)

	Test Product N (%)	Negative Control N (%)	Placebo 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)

	Test Product N (%)	Negative Control N (%)	Placebo N (%)	Overall N (%)
OTHER	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
SAFETY POPULATION	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
ITT POPULATION	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
PP POPULATION	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

Percentages for non-randomized category are based on number of screened subjects; percentages for randomized category are based on number of randomized subjects

PPD

Protocol 207656 Program Run Date:xxxx

Table 14.1.2
Analysis Populations
Randomized Population

Study Population: Randomized (N=xxx)

	Test Product N (%)	Negative Control N (%)	Placebo N (%)	Overall N (%)
SUBJECTS EXCLUDED FROM SAFETY POPULATION	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
REASON 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
REASON 2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
...				
SUBJECTS EXCLUDED FROM ITT POPULATION	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
REASON 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
REASON 2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
...				
SUBJECTS WITH AT LEAST ONE DATA POINT EXCLUDED FROM PP ANALYSIS	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
SUBJECTS COMPLETELY EXCLUDED FROM PP POPULATION	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
PROTOCOL DEVIATIONS LEADING TO EXCLUSION FROM PP				
All VISITS				
DEVIATION 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

	Test Product N (%)	Negative Control N (%)	Placebo N (%)	Overall N (%)
DEVIATION 2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
...				
WEEK4	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
DEVIATION 3	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
DEVIATION 4	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
...				
WEEK8	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
DEVIATION 5	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
DEVIATION 6	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
...				

Protocol 207656 Program Run Date:xxxx

Table 14.1.2.1
Subject Demographics and Baseline Characteristics
Safety Population

Study Population: Safety Population (N=XX)

	Test Product (N=XX)	Negative Control (N=XX)	Placebo (N=XX)	Overall (N=XX)
SEX n (%)				
MALE	xx (xx.x)	xx (xx.x)	...	xx (xx.x)
FEMALE	xx (xx.x)	xx (xx.x)	...	xx (xx.x)
RACE n (%)				
ASIAN	xx (xx.x)	xx (xx.x)	...	xx (xx.x)
BLACK or AFRICAN	xx (xx.x)	xx (xx.x)	...	xx (xx.x)
AMERICAN INDIAN OR ALASKA NATIVE	xx (xx.x)	xx (xx.x)	...	xx (xx.x)
NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	xx (xx.x)	xx (xx.x)	...	xx (xx.x)
WHITE	xx (xx.x)	xx (xx.x)	...	xx (xx.x)
MULTIPLE	xx (xx.x)	xx (xx.x)	...	xx (xx.x)
ETHNICITY N (%)				
HISPANIC OR LATINO	xx (xx.x)	xx (xx.x)	...	xx (xx.x)
NOT HISPANIC OR LATINO	xx (xx.x)	xx (xx.x)	...	xx (xx.x)
AGE (YEARS)				
n	XX	XX	...	XX

	Test Product (N=XX)	Negative Control (N=XX)	Placebo (N=XX)	Overall (N=XX)
MEAN	XX.X	XX.X	...	XX.X
SD	XX.XX	XX.XX	...	XX.XX
MEDIAN	XX.X	XX.X	...	XX.X
MINIMUM	XX	XX	...	XX
MAXIMUM	XX	XX	...	XX
STRATIFICATION				
MAXIMUM BASELINE SCHIFF SCORE 2				
	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
MAXIMUM BASELINE SCHIFF SCORE 3				
	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Protocol 207656 Program Run Date:xxxx

Table 14.2.1.1

Summary Statistics of Evaporative (Air) Schiff Sensitivity Score
Intent-to-Treat Population

Study Population: Intent to Treat (N=XXX)

		Test Product (N=XX)		Negative Control (N=XX)		Placebo (N=XX)	
Visit		Observed Value	Change from Baseline	Observed Value	Change from Baseline	Observed Value	Change from Baseline
BASELINE	N	XX		XX		XX	
	MEAN	X.XX		X.XX		X.XX	
	SD	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	
WEEK 4	N	XX	XX	XX	XX	XX	XX
	MEAN	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
	MEDIAN	X.X	X.X	X.X	X.X	X.X	X.X
	MINIMUM	X.X	X.X	X.X	X.X	X.X	X.X
	MAXIMUM	X.X	X.X	X.X	X.X	X.X	X.X
WEEK 8	SAME AS ABOVE						

Page x of y

PPD

Protocol 207656 Program Run Date:xxxx

Table 14.2.1.2
Statistical Analysis of Change from Baseline in Evaporative (Air) Schiff Sensitivity Score
Intent-to-Treat Population

Study Population: Intent to Treat (N=XXX)

	Test Product (N=XX)	Negative Control (N=XX)	Placebo (N=XX)
WEEK 4			
ADJUSTED MEAN [1]	XX.XX	XX.XX	XX.XX
SE [1]	XX.XXX	XX.XXX	XX.XXX
95% CI [1]	(XX.XXX, XX,XXX)	(XX.XXX, XX.XXX)	(XX.XXX, XX.XXX)
P-VALUE [1]	0.XXXX	0.XXXX	0.XXXX

COMPARISONS BETWEEN TREATMENTS	DIFFERENCE (SE) [1]	95% CI [1]	P-VALUE [1]
TEST PRODUCT VERSUS NEGATIVE CONTROL [1] *	XX.XX (XX.XXX)	(XX.XXX, XX.XXX)	0.XXX
TEST PRODUCT VERSUS PLACEBO [1]	XX.XX (XX.XXX)	(XX.XXX, XX.XXX)	0.XXX
TEST PRODUCT VERSUS COMBINED CONTROL [1,2]	XX.XX (XX.XXX)	(XX.XXX, XX.XXX)	0.XXX

WEEK 8 (AS ABOVE FOR WEEK 4)
...

* Test Product versus Negative Control at Week 8 is a primary endpoint comparision.
[1] From ANCOVA model with treatment as factor and baseline Schiff score as covariate. Difference is first named treatment minus second named treatment such that a negative difference favors the first named treatment.
[2] Test Product versus Combined Control (Placebo and Negative Control) group is obtained by using contrast.

Page x of y Program:

PPD

Programming Note: For Table 14.2.2.2 and 14.2.2.4: please update footnote [1] as

[1] From ANCOVA model with treatment and baseline Schiff stratification as factors and baseline tactile threshold as a covariate. Difference is the first named treatment minus second named treatment such that a positive difference favors the first named treatment.

For table Table 14.2.3.2 please update footnote [1] as

[1] From ANCOVA model with treatment and baseline Schiff stratification as factors and baseline VRS as a covariate. Difference is the first named treatment minus second named treatment such that a negative difference favors the first named treatment.

Protocol 207656 Program Run Date:xxxx

Table 14.3.1.1
Treatment Emergent Adverse Event by SOC and Preferred Term
Safety Population

Study Population: Safety Population (N=xx)

SOC Preferred Term	Test Product (N=XX)		Negative Control (N=XX)		Placebo (N=XX)		Overall (N=XX)	
	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.

PPD

Protocol 207656 Program Run Date:xxxx

Listing 16.1.7
Randomization Information
Randomized Population

Study Population: Randomized (N=xx)
Stratum 1: Maximum Schiff score =2

Subject Number	Age/Sex/ Race/Ethinicity[1]	Randomization Number	Planned Randomized Treatment	Actual Treatment Received	Date of Randomization
PPD					

[1] Age in years; Sex: F = Female, M = Male; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, M = Multiple; Ethinicity: H = Hispanic or Latino, NH = Not Hispanic or Latino

Page x of y

PPD

Protocol 207656 Program Run Date:xxxx

Listing 16.2.1.1
Subject Disposition
Randomized Population

Study Population: Randomized (N=xx)
Treatment Group: Test Product

Subject	Age/Sex/Race/ Ethinicity [1]	Screening Date	Treatment Start Date and Time [2]	Completion/ Withdrawal Date	Duration of Treatment (Days)	Completed?	Primary Reason for Withdrawal	Further Details [3]
PPD								

[1] Age in years; Sex: F = Female, M = Male; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, M = Multiple; Ethinicity: H = Hispanic or Latino, NH = Not Hispanic or Latino.
[2] Date and time of the brushing/rinsing with allocated treatment date at baseline visit.
[3] Further details of reasons for withdrawal.

Protocol 207656 Program Run Date:xxxx

Listing 16.2.1.2
Subject Disposition
Non-Randomized Subjects

Study Population: Non-Randomized (N=xx)

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

[1] Age in years; Sex: F = Female, M = Male; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, M = Multiple; Ethinicity: H = Hispanic or Latino, NH = Not Hispanic or Latino.
[2] Further details of reasons for screen failure.

Protocol 207656 Program Run Date:xxxx

Listing 16.2.2.1
Major Protocol Deviations
Randomized Population

Study Population: Randomized (N=xx)
Treatment Group: XXXXXX

Subject	Sex/Age/Race/ Ethinicity [1]	Week(s)Excluded from PP Population	Deviation Reason
PPD			

[1] Age in years; Sex: F = Female, M = Male; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, M = Multiple; Ethinicity: H = Hispanic or Latino, NH = Not Hispanic or Latino.

PPD

Protocol 207656 Program Run Date:xxxx

Listing 16.2.2.2
Minor Protocol Deviations
Randomized Population

Study Population: Randomized (N=xx)
Treatment Group: Test Product

Subject Number	Age/Sex/Race/ Ethinicity [1]	Visit	Deviation Sequence	Protocol Deviation
PPD				

[1] Age in years; Sex: F = Female, M = Male; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, M = Multiple; Ethinicity: H = Hispanic or Latino, NH = Not Hispanic or Latino.

PPD

Programming Note for Listing 16.2.2.2: Listing 16.2.2.2 lists only those identified in population definition document.

Protocol 207656 Program Run Date:xxxx

Listing 16.2.3.1
Exclusion from Analysis Population
Randomized Population

Study Population: Randomized (N=xx)

Subject Number	Age/Sex/Race/ Ethinicity [1]	Treatment Start Date and Time	Safety Population	ITT Population	PP population
PPD					

[1] Age in years; Sex: F = Female, M = Male; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, M = Multiple; Ethinicity: H = Hispanic or Latino, NH = Not Hispanic or Latino.

PPD

Programming Note for Listing 16.2.3: This listing is based on population definition document.

Protocol 207656 Program Run Date:xxxx

Listing 16.2.4.1
Demographic Characteristics
Randomized Popualtion

Study Population: Randomized (N=xx)
Treatment Group: Test Product

Subject Number	Age (years)	Sex	Race	Ethnicity	Stratum
PPD					

PPD

Protocol 207656 Program Run Date:xxxx

Listing 16.2.4.2
Medical History and Current Medical Conditions
Randomized Population

Study Population: Randomized (N=xx)
Treatment Group: Test Product

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

[1] Age in years; Sex: F = Female, M = Male; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, M = Multiple; Ethinicity: H = Hispanic or Latino, NH = Not Hispanic or Latino.

Protocol 207656 Program Run Date:xxxx

Listing 16.2.5.1
Concomitant Medications and Significant Non-drug Therapies Prior to Treatment
Randomized Population

Study Population: Randomized (N=xx)
Treatment Group: Test Product

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

[1] Age in years; Sex: F = Female, M = Male; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, M = Multiple; Ethinicity: H = Hispanic or Latino, NH = Not Hispanic or Latino.
[2] Study day relative to the date of Randomization.

Page x of y

PPD

Programming note: sort the listing by subject number, treatment start date.

Protocol 207656 Program Run Date:xxxx

Listing 16.2.6.1
Individual Efficacy Data for Schiff Sensitivity Score for Two Test Teeth
Randomized Population

Study Population: Randomized (N=xx)
Treatment Group: Test Product 1

Subject Number	Age/Sex/Race/ Ethinicity [1]	Tooth Number (Universal/FDI)	Timepoint	Score	Subject level Average	Change from Baseline
PPD						

[1] Age in years; Sex: F = Female, M = Male; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, M = Multiple; Ethinicity: H = Hispanic or Latino, NH = Not Hispanic or Latino.

PPD

Programming Note : 1) Subject level average is based raw values for selected 2 test teeth.

2) Please create a similar listsing for tactile and VRS score

Protocol 207656 Program Run Date:xxxx

Listing 16.2.7.1
All Adverse Events
Randomized Population

Study Population: Randomized (N=xx)
Treatment Group: Test Product 1

Subject Number	Age/Sex/ Race/ Ethinicity [1]	Adverse Event (Preferred Term) (System Organ Class)	Start Date /Study Day[2]	Start Time	End Date	End Time	Frequency /Intensity [3]	Related to Study Product?	Action Taken re Study Product	Outcome	Serious?	Withdrew? [4]
PPD		HEADACHE (NERVOUS SYSTEM DISORDER) [Non-Oral]	PPD			20:30	MILD	No	NOT APPLICABLE	RECOVERED/RESOLVED	NO	NO

@@ Adverse events with verbatim text ending in this are classified as Oral AEs.
[1] Age in years; Sex: F = Female, M = Male; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, M = Multiple; Ethinicity: H = Hispanic or Latino, NH = Not Hispanic or Latino.
[2] Study day is the day relative to start of treatment, day 1 being the day of first treatment.
[3] INT = Intermittent and SGLE = Single.
[4] Did subject withdraw from study as a result of this adverse event?

PPD

Programming Note for Listing 16.2.7.2:

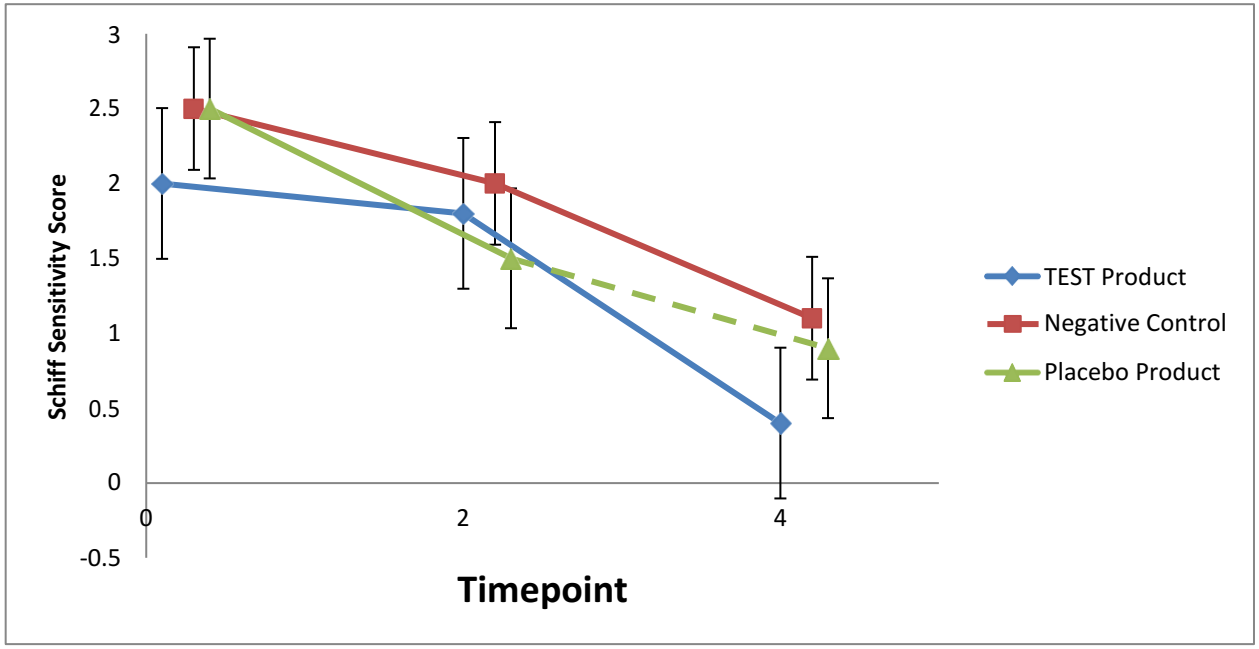
- *Repeat the same layout for listing 16.2.7.2*
- *Population should be used 'Non randomized Subjects'*
- *The fourth column should be only 'Start Date'*

- *Add footnote 'Only SAEs are collected for non randomized subjects'*
- *Delete the footnote related to study day and adjust the numbers accordingly.*

Protocol 207656 Program Run Date:xxxx

Figure 14.2.1
Evaporative (Air) Sensitivity Schiff Sensitivity Score by Time and Treatment
Intent to Treat Population

Study Population: Intent-to-Treat (N=XX)



*Mean and SE plotted are from summary statistics in T 14.2.1.1.1

Note to programmer: (1) Add 'Baseline', 'Week 4' and 'Week 8' to X-axis (2) Use different symbols and line-styles for three treatments (3) For Figures 14.2.4 & 14.2.5 use 'Per Protocol Population' in header.4. Please make sure that Y-axis scale should be 0-3 for Schiff score 5) 1) Please make sure that Y-axis scale should be 0-80 g for tactile