HALEON

STATISTICAL ANALYSIS PLAN

AN 8-WEEK, RANDOMIZED, CONTROLLED, EXAMINER-BLIND, CLINICAL STUDY TO EVALUATE THE EFFICACY OF A CALCIUM SODIUM PHOSPHOSILICATE TOOTHPASTE FOR THE RELIEF OF DENTIN HYPERSENSITIVITY IN A POPULATION OF DENTIN HYPERSENSITIVITY SUFFERERS

Protocol Number: 300100

Phase: N/A

This document contains confidentiality statements that are not relevant for this publicly available version

Document History

Document	Version Date	Summary of Changes (New analysis or Change in planned analysis)
Original Analysis Plan	28-Mar-2024	Not applicable (N/A)

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Abbreviations

Abbreviation	Term
AE	Adverse Events
BDRM	Blinded Data Review Meeting
CIs	Confidence Intervals
CRF	Case Report Form
CSPS	Calcium Sodium Phosphosilicate
DH	Dentin Hypersensitivity
DHEQ	Dentin Hypersensitivity Experience Questionnaire
EAR	Erosion/Abrasion/ Recession
eCRF	Electronic Case Report Form
ICF	Informed Consent Form
MedDRA	Medical Dictionary for Regulatory Activities
mITT	Modified Intent-To-Treat
MMRM	Mixed Model with Repeated Measures
N/A	Not Applicable
NRS	Numeric Rating Scale
OHRQoL	Oral health-related quality of life
OHT	Oral Hard Tissue
OST	Oral Soft Tissue
PP	Per-Protocol
PT	Preferred Term
SAE	Serious Adverse Events
SAP	Statistical Analysis Plan
SD	Standard Deviation
SE	Standard Error
SOC	System Organ Class
TEAEs	Treatment Emergent Adverse Events
WHODD	World Health Organization Drug Dictionary

The purpose of this Statistical Analysis Plan (SAP) is to describe the planned analyses and outputs to be included in the Clinical Study Report for Protocol 300100 (version 2.0, dated 06-Mar-2024).

1 Summary of Key Protocol Information

The purpose of this trial is to demonstrate the anti-sensitivity efficacy of a 5% Calcium Sodium Phosphosilicate (CSPS) toothpaste in a Dentin Hypersensitivity (DH) population. The clinical efficacy of the 5% CSPS toothpaste (Test Toothpaste) will be compared with that of a Reference Toothpaste, a commercially available, regular fluoride toothpaste with no known anti-sensitivity properties (negative control). The study will follow a single center, 8-week, randomized, controlled, examiner-blind, 2-treatment arm, parallel design, stratified (by maximum Baseline Schiff sensitivity score of the two selected 'Test Teeth'). Approximately 234 qualifying subjects will be stratified according to the maximum Baseline Schiff sensitivity score of their two 'Test Teeth' and randomized to treatment (approximately 117 subjects per treatment group).

At Screening (Visit 1), following provision of written Informed Consent Form (ICF), suitability to participate will be reviewed against the protocol inclusion/exclusion criteria. Eligible subjects will enter an acclimatization period (14-28 days) prior to Baseline assessments during which they will brush twice daily (morning and evening) with the acclimatization toothpaste (a different commercially available, regular fluoride toothpaste from the Reference Toothpaste). At Baseline (Visit 2), eligibility to continue will be assessed. Subjects who demonstrate the required qualifying levels of DH at Screening (Visit 1) and Baseline (Visit 2) will be randomized to study product and instructed to brush with their assigned investigational toothpaste twice daily (morning and evening) for the duration of the 8-week treatment period. DH will be assessed at Screening (Visit 1), Baseline (Visit 2), and after 3-, 7-, 14-, 28- and 56-days treatment (Visits 3-7) using two independent clinical measures: (i) tactile threshold (g) following a tactile stimulus and (ii) Schiff sensitivity score following an evaporative (air) stimulus.

Oral health-related quality of life (OHRQoL) will be monitored over the treatment period using the Dentin Hypersensitivity Experience Questionnaire (DHEQ-48), completed by study subjects at Baseline (Visit 2), and after 28- and 56-days treatment (Visits 6 and 7). At the final visit (Day 56), subjects will rate their level of satisfaction with their assigned investigational toothpaste for the overall management of their DH, using a Numeric Rating Scale (NRS). Safety and oral tolerability of the investigational toothpastes will be monitored over the 8-week usage period by review of treatment emergent adverse events (TEAEs).

1.1 Study Design

This will be a single center, 8-week, randomized, controlled, examiner-blind, 2-treatment arm, parallel group, stratified study in healthy subjects with DH. Subjects who meet the required

study criteria at Screening and Baseline will be randomized to one of two study products: a 5% CSPS toothpaste (Test Toothpaste) or a regular fluoride toothpaste (Reference Toothpaste).

Two independent stimulus-based clinical measures will be employed to assess the efficacy of the investigational toothpastes.

- A tactile stimulus will be administered using a constant pressure probe - Yeaple Probe (Polson, 1980); subject response to the stimulus determines the tactile threshold in grams (g).
- An evaporative (air) stimulus (i.e., a thermal stimulus) will be administered using a dental air syringe; subject response to the stimulus will be examiner-evaluated using the Schiff sensitivity scale (Schiff, 1994).

DH will be assessed at Screening, Baseline, Day 3, Day 7, Day 14, Day 28, and Day 56. On completion of the Baseline assessments, the clinical examiner will select two 'Test Teeth' for assessment of tactile and evaporative (air) sensitivity at all subsequent visits. To qualify for selection as a 'Test Tooth', the tooth must meet the protocol-specific dentition inclusion/exclusion criteria (Protocol Section 5.2 Inclusion Criteria 6 & 7; Section 5.3 Exclusion Criterion 26), specifically a tactile threshold $\leq$ 20g and a Schiff sensitivity score $\geq$ 2 at both Screening and Baseline visits.

Approximately 234 qualifying subjects will be stratified according to the maximum Baseline Schiff sensitivity score of their two 'Test Teeth' and randomized to treatment (approximately 117 subjects per treatment group). Randomized subjects will be instructed to brush twice daily (morning and evening) with their assigned investigational toothpaste for the next 56 days (8-weeks) and record each brushing in the diary provided. First use will be performed under supervision at the investigator site; to facilitate compliance throughout the treatment period, further supervised on-site brushings will be completed at Visits 3-6.

Changes in OHRQoL will be monitored over the treatment period using the validated DHEQ-48. The DHEQ-48 will be completed by study subjects at Baseline, and after 28- and 56-days treatment. At the final visit (Day 56), after all clinical procedures have been completed, subjects will rate their level of satisfaction with their assigned investigational toothpaste for the overall management of DH using a NRS.

To standardize oral hygiene practice in the study population prior to treatment and to help minimize the potential impact of 'placebo'/'no treatment' effects, eligible subjects will complete an acclimatization period (14-28 days duration) between the Screening and Baseline visits during which they will brush twice daily (morning and evening) with the regular fluoride toothpaste provided (a different commercially available product from the Reference Toothpaste). First use of acclimatization toothpaste will be performed under supervision at the investigator site.

Safety and oral tolerability of the investigational toothpastes will be monitored over the treatment period by review of TEAEs.

Table 1-1 presents the schedule of activities.

Table 1-1 Schedule of Activities

Procedure/Assessment	Study Visits						
	Visit 1 Screening	Visit 2 Day 0 Baseline	Visit 3 Day 3	Visit 4 Day 7	Visit 5 Day 14 (± 1 day)	Visit 6 Day 28 (± 2 days)	Visit 7 Day 56 (± 3 days)
Informed consent	X						
Demographics	X						
Review Subject's Oral Care Products	X						
Review Medical History & Current/Prior Concomitant Medication/Treatment [1]	x						
Review Changes in Health & Medications/Treatments [1]		x	x	x	x	x	x
Return Acclimatization Toothpaste, Toothbrush & Diary [2]		x					
Return Investigational Toothpaste, Toothbrush & Diary [2]							x
Compliance Checks [2]		x	x	x	x	x	x
Subject-Completed DHEQ [3]		x				x	x
Oral Soft Tissue (OST) Examination	x	x	x	x	x	x	x
Oral Hard Tissue (OHT) Examination	x						x
Eligible Teeth Assessments (Dentition Exclusions, Erosion/Abrasion/ Recession [EAR], Modified Gingival Index [MGI], Tooth Mobility)	x						
Qualifying Clinical Assessment of Tactile Sensitivity [4]	x	x					
Qualifying Clinical Assessment of Evaporative (Air) Sensitivity[5]	x	x					
Clinical Examiner Selects Two 'Test Teeth' (Qualifying Subjects Only) [6]		x					
Review Inclusion/Exclusion Criteria	x	x					

Acclimatization Period (14-28 days)

Procedure/Assessment	Study Visits						
	Visit 1 Screening	Visit 2 Day 0 Baseline	Visit 3 Day 3	Visit 4 Day 7	Visit 5 Day 14 (± 1 day)	Visit 6 Day 28 (± 2 days)	Visit 7 Day 56 (± 3 days)
Confirm Subject Eligibility/Qualification	x	x					
Dispense Acclimatization Toothpaste, Toothbrush, Timer, Rinsing Cups & Diary	x						
Supervised Brushing with Acclimatization Toothpaste	x						
Stratification/Randomization		x					
Dispense Investigational Toothpaste, Toothbrush, Rinsing Cups & Diary		x					
Supervised Brushing with Investigational Toothpaste		x					
Clinical Assessment of Tactile Sensitivity: Two 'Test Teeth' only [4]			x	x	x	x	x
Clinical Assessment of Evaporative (Air) Sensitivity: Two 'Test Teeth' only [5]			x	x	x	x	x
Supervised Brushing with Investigational Toothpaste			x	x	x	x	
Satisfaction with Treatment: Subject-Completed NRS							x
Study Conclusion							x
Monitor Adverse Events (AEs) and Medical Device Incidents [7]	x	x	x	x	x	x	x

AE= Adverse Events; DHEQ= Dentin Hypersensitivity Experience Questionnaire; OST= Oral Soft Tissue; OHT= Oral Hard Tissue; NRS= Numerical Rating Scale

Footnotes:

1. Female subjects of child-bearing potential should be asked to confirm pregnancy status at each visit.
2. Subjects will be required to bring their study supplies (minus timer & rinsing cups) to every visit.
   Perform visual check of returned study supplies, review diary & evaluate compliance:
   Visit 2: check compliance with use of acclimatization toothpaste; **Visits 3-7:** check compliance with use of investigational toothpaste.
   Visits 2-7: check compliance with Lifestyle Guidelines/Medication requirements.
3. DHEQ-48 must be completed prior to the OST examination and clinical assessments.
   Visit 2: Complete all questions; **Visits 6 & 7:** Complete Section 1, Q7-9 & Section 2, all questions.
4. **Tactile Threshold Assessment: Visits 1-2:** Maximum force 20g (Screening and Baseline); **Visits 3-7:** Maximum force 80g.
5. **Evaporative (air) sensitivity** should be assessed after tactile sensitivity; ensure minimum 5-minute delay after the last tactile assessment before the first evaporative (air) assessment for tooth recovery.

6. Selected 'Test Teeth' should be in different quadrants, with the requisite qualifying levels of DH at both Screening (Visit 1) and Baseline (Visit 2), i.e., tactile threshold ≤ 20g and Schiff sensitivity score ≥ 2.
7. AEs, and therefore all serious adverse events (SAEs), and incidents will be recorded from immediately after signing the ICF until 5 days after the last use of investigational toothpaste. Incidents will be recorded from first to last use of the medical device (the manual toothbrush used to apply the acclimatization and investigational toothpastes).

1.2 Study Objectives

Study objectives and endpoints are defined in Table 1-2:

Table 1-2 Study Objectives and Endpoints

Objectives	Endpoints
Efficacy	
Primary	
To demonstrate the clinical efficacy of a 5% CSPS toothpaste in reducing DH to an evaporative (air) stimulus (as measured by Schiff sensitivity score), compared to a negative control toothpaste, after 8 weeks twice daily use.	Change from Baseline in Schiff sensitivity score at Day 56 (Week 8).
Secondary	
To demonstrate the clinical efficacy of a 5% CSPS toothpaste in reducing DH to a tactile stimulus (as measured by tactile threshold in grams [g]), compared to a negative control toothpaste, after 8 weeks twice daily use.	Change from Baseline in tactile threshold (g) at Day 56 (Week 8).
To investigate the clinical efficacy of a 5% w/w CSPS toothpaste in reducing DH to evaporative (air) and tactile stimuli (as measured by Schiff sensitivity score and tactile threshold (g), respectively), compared to a negative control toothpaste, after 3-, 7-, 14- and 28-days twice daily use.	• Change from Baseline in Schiff sensitivity score at Days 3, 7, 14 & 28. • Change from Baseline in tactile threshold (g) at Days 3, 7, 14 & 28.
To describe subject-perceived changes in oral health-related quality of life (OHrQoL), as measured by the Dentin Hypersensitivity Experience Questionnaire (DHEQ-48), after 4- and 8-weeks twice daily use of their assigned investigational toothpaste.	At Day 28 (Week 4) & Day 56 (Week 8): Change from Baseline in DHEQ-48 endpoints. Section 1 • Impact on Everyday Life (Q7-9) Section 2 • Total Score (Q1-34) • Individual Domain Scores - Restrictions (Q1-4) - Adaptation (Q5-16) - Social Impact (Q17-21) - Emotional Impact (Q22-29)

Objectives	Endpoints
Efficacy	
	- Identity (Q30-34) • Global Oral Health Score (Q35) • Effect on Life Overall Score (Q36-39)
Exploratory	
To investigate subject satisfaction with their assigned investigational toothpaste for the overall management of DH, as measured by a Numeric Rating Scale (NRS), after 8 weeks treatment.	*At Day 56 (Week 8):* Satisfaction NRS score
Safety	
To monitor the safety and oral tolerability of the investigational toothpastes over 8 weeks twice daily use.	Treatment emergent adverse events (TEAEs).

This study will be considered successful if the 5% CSPS toothpaste demonstrates statistically significant, superior anti-hypersensitivity efficacy, compared to the negative control toothpaste, as measured by Schiff sensitivity score at Day 56 (Week 8).

1.3 Study Products

Table 1-3 presents the study products.

Table 1-3 Acclimatization/Investigational Toothpastes

Description	Acclimatization Toothpaste	Test Toothpaste	Reference Toothpaste (Negative Control)
Product Name	Regular fluoride toothpaste (Colgate Cavity Protection[1])	5.0 % w/w CSPS toothpaste	Regular fluoride toothpaste (Crest Cavity Protection[1])
Fluoride Level	1000 ppm fluoride[2]	1040 ppm fluoride[3]	1100 ppm fluoride[3]
Master Formulation Code (MFC)	N/A	CCI	N/A
Dispensing Details	One carton containing 2 tubes of toothpaste at Screening (Visit 1)	One carton containing 4 over-wrapped tubes of toothpaste at Baseline (Visit 2)	
Route of Administration	Topical Oral Use		
Toothpaste Usage Instructions	Dose the toothbrush with a ribbon of toothpaste, across the full brush head.		
	Start the timer (pre-set for 1-minute).		
	Brush the entire	Brush the entire dentition thoroughly for	Brush the entire dentition thoroughly

Description	Acclimatization Toothpaste	Test Toothpaste	Reference Toothpaste (Negative Control)
	dentition thoroughly for at least 1-timed minute, twice daily (morning & evening).	at least 1-timed minute, twice daily (morning & evening), making sure to brush the sensitive areas of the two 'Test teeth' carefully first.	for at least 1-timed minute, twice daily (morning & evening).
	Subjects who wish to rinse after brushing will be instructed to rinse with 10 mL water using graduated rinsing cup provided.		
Duration of Treatment	Approximately 8 weeks (56±3 days)		
Return Requirements	All used/unused tubes to be returned to the sponsor.		

CSPS: Calcium Sodium Phosphosilicate; N/A: Not Applicable

1. Commercially available daily use, regular fluoride toothpaste, US market.
2. As sodium monofluorophosphate
3. As sodium fluoride (NaF)

1.4 Sample Size Calculation

Sufficient subjects will be screened and entered into the acclimatization period to randomize approximately 234 subjects to study product (approximately 117 subjects per treatment group) to ensure approximately 210 complete the study (approximately 105 subjects per treatment group), allowing for approximately 10% dropouts.

The study will be sufficiently powered to demonstrate statistical superiority of the Test Toothpaste compared to the Reference Toothpaste (negative control) for the change from Baseline in the Schiff sensitivity score after 56 days, i.e., 8 weeks, (primary objective) and 3 days (key secondary objective, earliest time point) treatment. It is anticipated that the treatment effect will increase over time. A sample size of 105 evaluable subjects per treatment group will provide 90% power to detect a mean difference of 0.25 units (SD = 0.55) in change from Baseline in Schiff sensitivity score after 3 days treatment, using a 2-tailed 2-sample t-test with a 5% significance level. The sample size calculation was performed using PASS software version 23.0.1.

The dropout rate and SD estimates are based on the results of DH efficacy studies of similar design and duration (Clinical Studies CCI [redacted] and CCI [redacted] sponsor data held on file, available on request).

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:

- All subjects have completed the study as defined in the protocol.
- All required database cleaning activities including any external data reconciliation have been completed and database has been locked.
- 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 Day 0 (Visit 2) pre-treatment assessment with a non-missing value.

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

3.2 Subgroups/Stratifications

Subjects will be randomized into the study provided they have satisfied all subject selection criteria. Each qualifying subject will be stratified by the maximum Baseline Schiff sensitivity score of their two selected 'Test Teeth'. The stratification factor will give rise to two strata.

- **Stratum 1:** Maximum Schiff sensitivity score = 2.
- **Stratum 2:** Maximum Schiff sensitivity score = 3.

In the event of mis-stratification, the correct strata according to CRF information will be used in the analysis i.e. derived stratification variable from ADSL will be used for analysis.

3.3 Centers Pools

Since this is single center study, pooling of centres is not applicable.

3.4 Timepoints and Visit Windows

The timepoints and visits for this study are defined in the Table 1-1 "Schedule of Activities". Any deviation from the study schedule may be reviewed on case-by-case basis at the Blinded Data Review Meeting (BDRM) to determine whether the data should be excluded from the Per-Protocol (PP) analyses.

4 Data Analysis

Data analysis will be performed by CCI with oversight from Haleon. The statistical analysis software used will be SAS version 9.4 or higher.

Prior to database closure a BDRM will be conducted in which various aspects of the trial will be discussed and agreed.

Except as described below, 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 clinical study but are not subsequently randomized. An enrolled subject is a subject who has signed informed consent and is eligible to proceed beyond the screening visit.

The number of subjects screened, enrolled, and randomized subjects will be presented in Table 14.1.1.

The number and percentage of screen failure subjects (subjects not randomized) with reasons why subjects are not randomized will be displayed. Percentages for screen failure subjects will be based on the total number of subjects screened.

The number and percentage of randomized subjects who complete and discontinue the study, broken down by reason for discontinuation, by study product and overall will also be displayed. The percentages will be based on the number of subjects randomized.

Table 14.1.1 will also present the number and percentage of subjects in each of the defined analysis populations (as defined in Section 4.1.3) by study product and overall. Percentages will be based on the number of subjects randomized.

Subject disposition including demographic data (age, sex, race and ethnicity), screening date, study product start date and time, subject status (completer, Yes/No), study completion /withdrawal date, duration (in days) in the study (defined as [(date of completion or withdrawal – start date of study product) + 1], and the primary reason for withdrawal will be listed (Listing 16.2.1.1) by study product.

Subject disposition information will be listed for non-randomized subjects (Listing 16.2.1.2), displaying subject number, demographic information (age, sex, race, and ethnicity), screening date, reason for screen failure and any further details of reason for screen.

4.1.2 Protocol Deviations

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 categorised. Subjects with important protocol deviations liable to

influence the efficacy outcomes will have affected data excluded from the PP analyses. Subjects may also be identified as having important protocol deviations not leading to exclusion of data from the PP analyses.

Important deviations of the protocol procedures may include, but will not necessarily be limited to the following:

- Consent procedures
- Inclusion/Exclusion criteria
- Concomitant medication/therapy
- Study procedures
- Randomization procedures
- Study drug dosing/study product administration/study product compliance Visit schedule/interval
- Other

The specific details of the important protocol deviations will be listed in Protocol Deviation Management Plan and assessment process will be specified in the Blind Data Review Plan and subjects with important protocol deviations will be identified at the BDRM.

The number and percentage of subjects with at least one important protocol deviation, subjects with important protocol deviations not leading to exclusion from PP population with reasons for deviations and subjects with important protocol deviations leading to exclusion from the PP population with reasons for deviations will be presented by study product and overall, for all randomized subjects (Table 14.1.2) and listed in Listing 16.2.2.1.

All protocol deviations collected on the protocol deviation case report form page will be listed in Listing 16.2.2.2. The listing will present date of deviation, type of deviation, and deviation description.

4.1.3 Analysis Populations

Three analysis populations are defined.

Population	Definition / Criteria	Analyses Evaluated
Safety	Comprise of all randomized subjects who receives at least one dose of study product. Any subject who receives a randomization number will be considered to have been randomized. This population will be based on the treatment the subject actually received.	• Safety
Modified Intent-To-Treat (mITT)	Comprise all randomized subjects who complete at least one dose of study product and have at least one post-baseline DH efficacy assessment.	• Demographic • Baseline Characteristics • Efficacy Analysis

Population	Definition / Criteria	Analyses Evaluated
	Any subject who receives a randomization number will be considered to have been randomized. This population will be based on the study product to which the subject was randomized.	
Per-Protocol	Comprise all subjects in the mITT population who have at least one DH efficacy assessment considered to be unaffected by protocol deviations. Protocol deviations that would exclude subjects from the PP population are defined in Section 4.1.2 (Protocol Deviations). This population will be based on the study product to which the subject was randomized.	• Efficacy Analysis

NOTES :
Please refer to Appendix 1: List of Data Displays which details the population to be used for each displays being generated.

The numbers of subjects included in each of the analysis populations will be summarized (Table 14.1.1). Subjects excluded from any of the analysis populations will be listed in Listing 16.2.3.1, with the reason for exclusion.

The primary population for assessment of efficacy will be the mITT Population. A PP analysis will be performed on the DH endpoints. If at least 10% of the mITT subjects are excluded from the PP Population, a decision on whether a PP analysis will be performed will be made prior to study unblinding (release of the randomization codes).

4.2 Subject Demographics and Other Baseline Characteristics

4.2.1 Demographic and Baseline Characteristics

Descriptive statistics (number of subjects [n], mean, standard deviation [SD], median, minimum, and maximum for continuous variables and frequency count [n] and percentage [%] of subjects for categorical variables) will be presented for demographic characteristics by study product and overall. These variables include age, sex, race, ethnicity, and stratification group and will be presented for the Safety population (Table 14.1.3.1) and the mITT population (Table 14.1.3.2).

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

4.2.2 General Medical History

Medical and surgical history (in the last year) including allergies or drug sensitivity will be listed in Listing 16.2.4.2, with start date and end date or ongoing at the start of study product.

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

Randomization details will be listed, including the randomization number, stratification group, the planned study product, the actual study product the subject was randomized to and the randomization date (Listing 16.1.7.1) for all randomized subjects.

4.3.1 Study Product Compliance and Exposure

Compliance data will also be summarized for the mITT population and will be assessed by number of brushings.

Number of actual brushings, brushing compliance (%), number of missed brushings, number of additional brushings will be summarized using descriptive statistics by cumulative visit and by study product (Table 14.2.1).

Number of actual brushings is defined as: [(date of Visit *x*– date of Visit 2) multiplied by 2 – number of missing brushings + number of additional brushings], where x = 3, 4, 5, 6 and 7, respectively.

Brushing compliance (%) is defined as: [100 × (Number of actual brushings / Expected number of brushings)], where expected number of brushings is defined as: [(date of Visit x – date of Visit 2) multiplied by 2].

Study product compliance (number of brushings / brushing compliance [%] / number of missed brushings / numbers of additional brushings) will be listed in Listing 16.2.5.1 for all randomized subjects by study product.

Supervised study product application (subject number, date of visit and time of the supervised procedure) will be listed (Listing 16.2.5.2) for all randomized subjects.

4.3.2 Prior and Concomitant Medication

Prior medications/treatments, including prescription and non-prescription drugs, dietary supplements and herbal remedies, taken in the last 30 days and prior to signing the informed consent form, will be documented in the CRF. The prior and concomitant medications will be coded using a validated medication dictionary, World Health Organization Drug Dictionary (WHODD).

Prior medications and prior non-drug treatments will be listed by subject, with drug name, WHODD Drug Synonym, reason for medication, route, dose, frequency, start date, start day relative to the study product start date, end date and end day relative to the study product start date (Listing 16.2.4.3) for all safety subjects. Prior medications are defined as those which stopped before the first use of the study product.

Concomitant medications and concomitant non-drug therapies taken during treatment will be listed similarly (Listing 16.2.4.4) for all safety subjects with either ongoing or end date

displayed. Concomitant medications are defined as medications that started or stopped on or after the first use of the study product or are ongoing.

Unknown dates will not be imputed. However, if the start or stop date is unknown, then it will be assumed to be concomitant medication unless the partial start date or stop date indicates differently.

4.4 Analysis of Efficacy

The primary population for assessment of efficacy will be the mITT Population.

All p-values presented will be two-sided and assessed at the 5% significance level. A sequential testing strategy will be used to adjust for multiplicity for the comparisons between the Test and Reference Toothpastes in change from Baseline in Schiff sensitivity score and tactile threshold (g) at each assessment time point.

At each timepoint, change from Baseline in tactile threshold (g) will only be assessed for confirmatory evidence if the change from Baseline in Schiff sensitivity score achieves a statistically significant greater reduction for the Test Toothpaste compared to Reference Toothpaste (negative control). This strategy will begin at Day 56, then move to successively earlier timepoints (i.e., Day 56 →Day 28 → Day 14 → Day 7 → Day 3), only moving the next earlier timepoint for confirmatory evidence if all later timepoints achieve statistically significant greater reductions for the Test Toothpaste compared to Reference Toothpaste (negative control) for both Schiff sensitivity score and tactile threshold (g). There will be no further adjustments for multiplicity for the other secondary endpoints (DHEQ-48).

The results from each MMRM will be tabulated, presenting the following information, in addition to the results specified for the primary and secondary analyses below: least square mean change from Baseline for each study product at Days 3, 7, 14, 28 and 56 (based on the observed stratification margins for those MMRM with a term for randomized strata) and used to test for any change from Baseline, with two-sided p-values and 95% CIs.

4.4.1 Primary Efficacy Endpoint

4.4.1.1 Change from Baseline in Schiff Sensitivity Score at Day 56

The primary efficacy variable is the change from Baseline in Schiff sensitivity score at Day 56.

Schiff sensitivity score will be derived as the mean score for the two 'Test Teeth' (selected at Baseline). Change from Baseline will be derived for each individual tooth first before calculating mean change for the two 'Test Teeth' where change from Baseline in Schiff sensitivity score at Day *x* is defined as [(Schiff sensitivity score at Day *x*) minus (Baseline Schiff sensitivity score)].

Descriptive statistics (n, mean, SD, standard error [SE], median, minimum, and maximum) will be presented for Schiff sensitivity score calculated as the average score of the two test teeth at

each assessment time point in Table 14.2.2.1.1 for all subjects in mITT population by study product. Raw means (± SE) of the Schiff sensitivity score at each time point will be plotted by study product in Figure 14.2.2.1.1 for all subjects in mITT population.

Individual Schiff sensitivity score data will be listed for each subject by visit and study product group in Listing 16.2.6.1 and Listing 16.2.6.2, for Screening and Baseline, and separately for two test teeth respectively, for all randomized subjects.

4.4.1.2 Statistical Hypothesis, Model, and Method of Analysis

The following null and alternative hypotheses will be evaluated:

- H_0: There is no difference in change from baseline in Schiff sensitivity score in the Test Toothpaste compared to Reference Toothpaste
- H_1: There is a difference in change from baseline in Schiff sensitivity score in the Test Toothpaste compared to Reference Toothpaste

Change from Baseline in Schiff sensitivity score at Day 56 will be analysed using a MMRM with study product, visit and [study product x visit] interaction as fixed effects, and Baseline Schiff sensitivity score as a 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. Subject will be included as a repeated measure with unstructured covariance matrix. Kenward-Roger's degrees of freedom approach will be applied (Kenward, 1997). The difference between the least square mean changes from Baseline for the Test Toothpaste compared to Reference Toothpaste (negative control) at Day 56 from the MMRM will be presented, along with the two-sided p-value and 95% CIs. In the event that the model does not converge on the unstructured covariance matrix, an appropriate alternative will be considered.

Using the above model, the adjusted mean change from baseline in the Schiff sensitivity score will be reported by study product along with 95% confidence intervals (CIs) and p-values testing for a non-zero change from baseline and will be provided in Table 14.2.2.2.1. Also, mean differences between Test Toothpaste compared to the Reference Toothpaste in the change from baseline in Schiff sensitivity score at Day 56 will be presented along with 95% CIs and p-values in the same Table 14.2.2.2.1.

The assumptions of normality and homogeneity of variance in the MMRM will be investigated. In case of violation of these assumptions, a suitable non-parametric test (Van Elteren Test, adjusted for the randomization stratification, Maximum Baseline Schiff sensitivity score) will be performed to assess the change from Baseline comparison (Test Toothpaste vs. Reference Toothpaste at Day 56); the results will be provided to support the MMRM results.

4.4.1.3 Supportive Analyses

If there is at least 10% difference in the overall number of subjects between PP and mITT Populations, a summary and statistical analysis of the Schiff sensitivity score will be presented

for the PP Population in Table 14.2.2.1.2 and Table 14.2.2.2.2, respectively. In addition, Schiff sensitivity score (Figure 14.2.2.1.2) at each time point will be plotted by study product in for all subjects in PP Population.

A decision on whether a PP analysis will be performed will be made prior to study unblinding (release of the randomization codes).

4.4.2 Secondary Efficacy Endpoints

4.4.2.1 Change from Baseline in Tactile Threshold (g) at Day 56

The key secondary variable is the change from Baseline in tactile threshold (g) at Day 56.

Tactile threshold (g) will be derived as the mean value for the two 'Test Teeth' (selected at Baseline). Change from Baseline will be derived for each individual tooth first before calculating mean change for the two 'Test Teeth' where change from Baseline in tactile threshold (g) at Day *x* is defined as [(tactile threshold at Day *x*) minus (Baseline tactile threshold)].

Descriptive statistics (n, mean, SD, standard error [SE], median, minimum, and maximum) will be presented for tactile threshold (g) calculated as the average score of the two test teeth at each assessment time point in Table 14.2.3.1.1 for all subjects in mITT population by study product. Raw means (± SE) of the tactile threshold (g) at each time point will be plotted by study product in Figure 14.2.2.2.1 for all subjects in mITT population.

Individual tactile threshold (g) data will be listed for each subject by visit and study product group in Listing 16.2.6.3 and Listing 16.2.6.4, for Screening and Baseline, and separately for two test teeth respectively, for all randomized subjects.

4.4.2.1.1 Statistical Hypothesis, Model and Method of Analysis

The following null and alternative hypotheses will be evaluated:

- H_0: There is no difference in change from baseline in tactile threshold (g) in the Test Toothpaste compared to Reference Toothpaste
- H_1: There is a difference in change from baseline in tactile threshold (g) in the Test Toothpaste compared to Reference Toothpaste

Key secondary endpoint, change from Baseline in tactile threshold (g) at Day 56, will be analysed using the same MMRM method detailed in Section 4.4.1.2 but with Baseline tactile threshold (g) as a covariate (rather than Baseline Schiff sensitivity score). In addition, the maximum Baseline Schiff sensitivity score of the two 'Test Teeth' (2 or 3) will be fitted as a fixed effect. The results will be presented in Table 14.2.3.2.1.

4.4.2.1.2 Supportive Analyses

A PP analysis will be performed on the change from baseline in tactile threshold (g) as detailed in Section 4.4.1.3 and the same MMRM model will be used as detailed in Section 4.4.2.1.1. The results will be presented in Table 14.2.3.1.2 and Table 14.2.3.2.2 respectively for summary table and analysis table. Also, Figure 14.2.2.2.2 will be generated for all subjects in PP population.

4.4.2.2 Change from Baseline in Schiff Sensitivity Score at Day 28, Day 14, Day 7, and Day 3

The other secondary efficacy endpoint will be the change from Baseline in Schiff sensitivity score at Day 28, Day 14, Day 7, and Day 3.

The summary results for this endpoint will be obtained as detailed in Section 4.4.1.1. The results will be presented in Table 14.2.2.1.1.

4.4.2.2.1 Statistical Hypothesis, Model and Method of Analysis

The analysis is same as primary endpoint and the details will be obtained from Section 4.4.1.2. Also, the results will be presented in Table 14.2.2.2.1.

4.4.2.2.2 Supportive Analyses

A PP analysis will be performed on the change from baseline in Schiff sensitivity score as detailed in Section 4.4.1.3 and the same MMRM model will be used as detailed in Section 4.4.1.2. The results will be presented in Table 14.2.2.1.2 and Table 14.2.2.2.2 respectively for summary table and analysis table. Also, Figure 14.2.2.1.2 will be generated for all subjects in PP population.

4.4.2.3 Change from Baseline in Tactile Threshold (g) at Day 28, Day 14, Day 7, and Day 3

The other secondary efficacy endpoint will be the change from Baseline in tactile threshold (g) at Day 28, Day 14, Day 7, and Day 3.

The summary results for this endpoint will be obtained as detailed in Section 4.4.2.1. The results will be presented in Table 14.2.3.1.1.

4.4.2.3.1 Statistical Hypothesis, Model and Method of Analysis

The analysis is same as the key secondary endpoint and the details will be obtained from the MMRM detailed in Section 4.4.2.1.1. Also, the results will be presented in Table 14.2.3.2.1.

4.4.2.3.2 Supportive Analyses

A PP analysis will be performed on the change from baseline in tactile threshold (g) as detailed in Section 4.4.2.1.2. The results will be presented in Table 14.2.3.1.2 and Table 14.2.3.2.2

respectively for summary table and analysis table. Also, Figure 14.2.2.2.2 will be generated for all subjects in PP population.

4.4.2.4 Change from Baseline in DHEQ-48 endpoints at Day 56 and Day 28

DHEQ-48:

The DHEQ-48 is a condition-specific measure of OHrQoL in relation to DH (Boiko, 2010) that has been previously validated in longitudinal studies and shown to be responsive to treatment (Baker, 2014). The DHEQ total score can be broken down into 5 separate 'domain' scores to provide a more granular understanding of the specific areas of improvement subjects experience in their OHrQOL.

- **Restrictions:** Derived from participant responses to Section 2, Q1-4 ('the ways in which any sensations in your teeth affect you in your daily life').
- **Adaptation:** Derived from participant responses to Section 2, Q5-16 ('the ways in which the sensations in your teeth have forced you to change things in your daily life'; 'things you do in your daily life to avoid experiencing the sensations in your teeth').
- **Social Impact:** Derived from participant responses to Section 2, Q17-21 ('the way the sensations affect you when you are with other people or in certain situations').
- **Emotional Impact:** Derived from participant responses to Section 2, Q22-29 ('the way the sensations in your teeth make you feel').
- **Identity:** Derived from participant responses to Section 2, Q30-34 ('what the sensations in your teeth mean for you').

The DHEQ also provides specific information on how much the sensations in the participant's teeth affect their life overall:

- **Global Oral Health:** Derived from participant response to Section 2, Q35 ('rate the health of your mouth, teeth and gums').
- **Effect on Life Overall:** Derived from participant responses to Section 2, Q36-39 (impact of DH on overall quality of life).

The other secondary efficacy endpoints will be the change from baseline in DHEQ-48 endpoints (as described below) at respective visits for each study product.

Change from Baseline will be calculated at Day 28 and Day 56 for all DHEQ endpoints.

Section 1

1. Impact on Everyday Life: Q7, Q8 & Q9 (separate scores)

Section 2

1. DHEQ Total Score (sum of Q1-34)
2. DHEQ Restrictions Domain score (sum of Q1-4)

3. DHEQ Adaptation Domain score (sum of Q5-16)
4. DHEQ Social Impact Domain score (sum of Q17-21)
5. DHEQ Emotional Impact Domain score (sum of Q22-29)
6. DHEQ Identity Domain score (sum of Q30-34)
7. DHEQ Global Oral Health Score (Q35)
8. DHEQ Effect on Life Overall Score (sum of Q36-Q39)

Change from Baseline will be calculated at the subject-level first then mean change from Baseline will be calculated for each DHEQ endpoint (mentioned above) across all subjects.

Descriptive statistics (n, mean, SD, standard error [SE], median, minimum, and maximum) will be presented for each DHEQ-48 endpoint (mentioned above) at each assessment time point in Table 14.2.4.1.1 and 14.2.5.1-8.1.1, for Section 1 and Section 2 respectively and for all subjects in mITT population by study product. Raw means (± SE) for each DHEQ endpoint, and the individual DHEQ questions, at each assessment will be plotted by study product in Figure 14.2.3.1 and Figure 14.2.2.3-10.1, for Section 1 and Section 2 respectively and for all subjects in mITT population.

Individual DHEQ endpoint data for each endpoint (mentioned above) will be listed for each subject by visit and study product group in Listing 16.2.6.5, 16.2.6.6.1-7, for Section 1 and Section 2 respectively, for all randomized subjects.

4.4.2.4.1 Statistical Hypothesis, Model and Method of Analysis

The following null and alternative hypotheses will be evaluated:

- H_0: There is no difference between baseline and post-baseline (Day 28, Day 56)
- H_1: There is a difference between baseline and post-baseline (Day 28, Day 56)

Change from Baseline for each DHEQ endpoint listed above will be analyzed using a MMRM with visit and stratification [maximum Baseline Schiff sensitivity score of the two 'Test Teeth' (2 or 3)] as fixed effects, and the respective Baseline DHEQ score as a covariate. Subject will be included as a repeated measure with unstructured covariance matrix. Kenward-Roger's degrees of freedom will be applied. The estimates of the adjusted mean (SE) change from Baseline will be presented along with 95% CIs for each treatment group. In the event that the model does not converge on the unstructured covariance matrix, an appropriate alternative will be considered.

Using the above model, the adjusted mean change from baseline in each DHEQ endpoint listed above will be reported by study product group along with 95% CIs and p-values testing for a non-zero change from baseline will be provided in Table 14.2.4.2.1 and 14.2.5.1-8.2.1, for Section 1 and Section 2 respectively.

The assumptions of normality and homogeneity of variance in the MMRM will be investigated. In case of violation of these assumptions, a suitable non-parametric test (Wilcoxon Signed Rank Test) will be performed to assess the change from Baseline comparison (Post-Baseline vs. Baseline); the results will be provided to support the MMRM results.

4.4.2.4.2 Supportive Analyses

If there is at least 10% difference in the overall number of subjects between PP and mITT Populations, a summary and statistical analysis of each of the DHEQ-48 Score endpoint will be presented for the PP Population in (Table 14.2.4.1.2 and 14.2.5.1-8.1.2 for Section 1 and Section 2 respectively) and (Table 14.2.4.2.2 and 14.2.5.1-8.2.2 for Section 1 and Section 2 respectively), respectively for summary table and analysis table. In addition, DHEQ-48 score (Figure 14.2.3.2 and Figure 14.2.2.3-10.2 for Section 1 and Section 2 respectively) for each mentioned endpoint at each time point will be plotted by study product in for all subjects in PP Population.

A decision on whether a PP analysis will be performed will be made prior to study unblinding (release of the randomization codes).

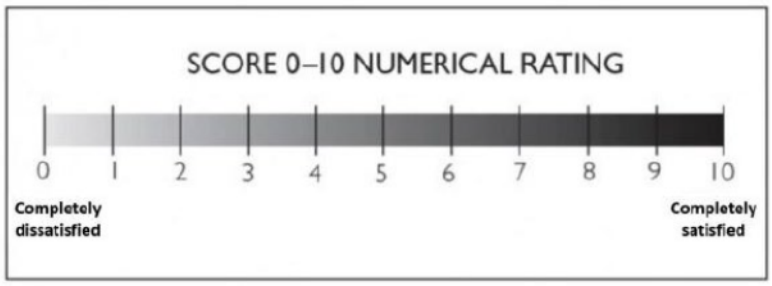
4.4.3 Exploratory Efficacy Variables

Satisfaction with Treatment using Numeric Rating Scale:

At the end of the study (Visit 7), subjects will be asked to rate their level of satisfaction with their allocated study product using a NRS. The NRS is an 11-point ordinal scale used to assess the subject's satisfaction with the product's overall management of their DH. The scale ranges from 0 (completely dissatisfied) to 10 (completely satisfied), with higher scores indicative of greater satisfaction (van Berckel, 2017):See example below:

Subjects will be asked to record the numeric value on the segmented scale that best describes their level of satisfaction after 8 weeks twice daily use and indicate why they selected a particular score in answer to the question 'Please give more details on why you are satisfied or dissatisfied with the product' (free text response).

Figure 4-1 Numerical Rating Scale (0 to 10)



4.4.3.1 Satisfaction NRS Score

Descriptive statistics (n, mean, SD, standard error [SE], median, minimum, and maximum) will be presented for NRS Score at Day 56 in Table 14.2.5.9.2 for all subjects in mITT population by study product.

Also, summary of the number of subjects (%) reporting at each level of the NRS and the cumulative number of subjects (%) reporting at each level or higher at Day 56 will be presented in Table 14.2.5.9.1 by study product.

4.4.3.1.1 Statistical Hypothesis, Model and Method of Analysis

No formal statistical analysis is planned for assessment of NRS endpoint.

4.4.4 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.

The use of MMRM analyses account for missing data assuming a missing at random assumption, i.e., there is a systematic relationship between the propensity of missing values and the observed data, but not the missing data.

It is therefore assumed that a subject with missing data at one post-Baseline assessment visit would have obtained a similar efficacy result at that visit compared to a subject using the same study product with similar non-missing results at other timepoints (Baseline and the other post-Baseline assessment visits). Sensitivity analyses may be added to the SAP prior to unblinding in case of high drop-out rates and/or exclusion from PP analyses.

4.5 Analysis of Safety

The safety profile of the study products will be assessed with respect to AEs or incidents and OST/OHT abnormalities in oral health study.

4.5.1 Adverse Events and Serious Adverse Events

All AEs will be reviewed by the Clinical Research Scientist or Designee prior to database lock and will be coded to a system organ class (SOC) and preferred term (PT) using the Medical Dictionary for Regulatory Activities (MedDRA).

AEs will be classified as oral and non-oral on the AE page of eCRF.

Treatment emergent adverse events (TEAEs) are defined as new AEs that occur on or after the first study product use (if this date is missing a suitable alternative will be used e.g., date of randomization). AEs with an onset date/time prior to the first study product use will be considered as non-treatment emergent.

The following summary tables and listings will be presented by study product.

- Table of TEAEs by SOC and PT (Table 14.3.1.1).
- Table of TEAEs by Oral/Non-Oral and PT (Table 14.3.1.2)
- Table of treatment related TEAEs by SOC and PT (Table 14.3.1.3)
- Table of treatment related TEAEs by Oral/Non-Oral and PT (Table 14.3.1.4)
- Listing of all AEs (Listing 16.2.7.1 for safety population)
- Listing of deaths (Listing 14.3.2.1)
- Listing of non-fatal SAEs (Listing 14.3.2.2)
- Listing of TEAEs leading to study or drug discontinuation (Listing 14.3.2.3)
- Listing of TEAEs classified as Oral (Listing 14.3.2.4)

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

All incidents will be listed in Listing 16.2.7.2. In the event that there is nothing to report, a null listing will be produced.

4.5.2 Other Safety Variables

Other safety variables are listed below:

- OST examination
- OHT examination

4.5.2.1 OST Examination

This procedure will be conducted by a qualified, experienced clinical examiner. The OST examination will be accomplished by direct visual observation and palpation, using retraction aids as appropriate, and will include examination of the labial mucosa (including lips), buccal mucosa, mucogingival folds, gingival mucosa, hard palate, soft palate, tonsillar area, pharyngeal area, tongue, sublingual area, submandibular area and salivary glands. The results of the examination will be recorded in the eCRF as either 'normal' or 'abnormal'; details of any abnormalities will be documented in the eCRF.

Any observation that changes from 'normal' to 'abnormal', or worsens, from the OST examination completed at Screening will be recorded as an AE.

OST will be summarized (number of subjects and percentages with abnormalities, without abnormalities, or OST not examined) by visit and study product in Table 14.3.4.1 for all subjects in Safety Population. OST examination will be listed (Listing 16.2.8.1) for Safety Population.

4.5.2.2 OHT Examination

This procedure should be conducted by a qualified, experienced clinical examiner. The OHT examination will be accomplished by direct visual observation, using retraction aids as appropriate, and will identify enamel irregularities, tooth fractures, grossly carious lesions/gross decay, defective/faulty restorations (both direct and indirect restorations, including fixed/

removable prostheses), non-carious tooth surface loss (abrasion, attrition, abfraction and erosion), any other hard tissue irregularities (e.g., hypo- and hypermineralization, decalcification) and significant tooth staining. Observations will be listed as 'absent' or 'present'; conditions noted as 'present' will be described in the eCRF.

Any observation that changes from 'absent' to 'present' or worsens from the OHT examination completed at Screening will be recorded as an AE. The presence of any implants, fixed or removable dentures, fixed or removable orthodontic braces/bands, fixed orthodontic retainers, full crowns or veneers will be recorded, along with evidence of gross intra-oral neglect or the need for extensive dental therapy.

OHT examination will be listed (Listing 16.2.8.2) for safety population.

4.6 Analysis of Other Variables

N/A.

5 Changes to the Protocol Defined Statistical Analysis Plan

There were no changes to the originally planned statistical analysis specified from the protocol version 2.0 (Dated: 06-Mar-2024).

Appendix 1: List of Data Displays

CSR Section	TLF	Number	Title	Population	Template	Topline
14.1 Demographic Data Summary Tables and Figures						
	Table	14.1.1	Subject Disposition	All Screened Subjects	14.1.1	Yes
	Table	14.1.2	Incidence of Important Protocol Deviations	All Randomized Subjects	14.1.2	
	Table	14.1.3.1	Demographic and Baseline Characteristics	Safety Population	14.1.3.1	
	Table	14.1.3.2	Demographic and Baseline Characteristics	mITT Population	14.1.3.1	Yes
14.2 Efficacy Data Summary Tables and Figures						
	Table	14.2.1	Summary of Brushing Compliance	mITT Population	14.2.1	
	Table	14.2.2.1.1	Summary of Schiff Sensitivity Score of the Two Test Teeth	mITT Population	14.2.2.1.1	Yes
	Table	14.2.2.1.2	Summary of Schiff Sensitivity Score of the Two Test Teeth	PP Population	14.2.2.1.1	
	Table	14.2.2.2.1	Statistical Analysis of Change from Baseline in Schiff Sensitivity Score of the Two Test Teeth Over Time	mITT Population	14.2.2.2.1	Yes
	Table	14.2.2.2.2	Statistical Analysis of Change from Baseline in Schiff Sensitivity Score of the Two Test Teeth Over Time	PP Population	14.2.2.2.1	
	Table	14.2.3.1.1	Summary of Tactile Threshold (g) of the Two Test Teeth	mITT Population	14.2.3.1.1	Yes
	Table	14.2.3.1.2	Summary of Tactile Threshold (g) of the Two Test Teeth	PP Population	14.2.3.1.1	
	Table	14.2.3.2.1	Statistical Analysis of Change from Baseline in Tactile Threshold (g) of the Two Test Teeth Over Time	mITT Population	14.2.3.2.1	Yes

CSR Section	TLF	Number	Title	Population	Template	Topline
	Table	14.2.3.2.2	Statistical Analysis of Change from Baseline in Tactile Threshold (g) of the Two Test Teeth Over Time	PP Population	14.2.3.2.1	
	Table	14.2.4.1.1	Summary of DHEQ (Section 1 Impact of Everyday Life, Q7 to Q9)	mITT Population	14.2.4.1.1	
	Table	14.2.4.1.2	Summary of DHEQ (Section 1 Impact of Everyday Life, Q7 to Q9)	PP Population	14.2.4.1.1	
	Table	14.2.4.2.1	Statistical Analysis of Change from Baseline in DHEQ (Section 1 Impact of Everyday Life, Q7 to Q9)	mITT Population	14.2.4.2.1	
	Table	14.2.4.2.2	Statistical Analysis of Change from Baseline in DHEQ (Section 1 Impact of Everyday Life, Q7 to Q9)	PP Population	14.2.4.2.1	
	Table	14.2.5.1.1.1	Summary of DHEQ (Section 2, Q1 to Q34) Total Score	mITT Population	14.2.5.1.1.1	
	Table	14.2.5.1.1.2	Summary of DHEQ (Section 2, Q1 to Q34) Total Score	PP Population	14.2.5.1.1.1	
	Table	14.2.5.1.2.1	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q1 to Q34) Total Score Over Time	mITT Population	14.2.5.1.2.1	
	Table	14.2.5.1.2.2	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q1 to Q34) Total Score Over Time	PP Population	14.2.5.1.2.1	
	Table	14.2.5.2.1.1	Summary of DHEQ (Section 2, Q1 to Q4) Restriction Domain Total Score	mITT Population	14.2.5.2.1.1	
	Table	14.2.5.2.1.2	Summary of DHEQ (Section 2, Q1 to Q4) Restriction Domain Total Score	PP Population	14.2.5.2.1.1	
	Table	14.2.5.2.2.1	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q1 to Q4) Restriction Domain Total Score	mITT Population	14.2.5.2.2.1	
	Table	14.2.5.2.2.2	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q1 to Q4) Restriction Domain Total Score	PP Population	14.2.5.2.2.1	

CSR Section	TLF	Number	Title	Population	Template	Topline
	Table	14.2.5.3.1.1	Summary of DHEQ (Section 2, Q5 to Q16) Adaptation Domain Total Score	mITT Population	14.2.5.3.1.1	
	Table	14.2.5.3.1.2	Summary of DHEQ (Section 2, Q5 to Q16) Adaptation Domain Total Score	PP Population	14.2.5.3.1.1	
	Table	14.2.5.3.2.1	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q5 to Q16) Adaptation Domain Total Score	mITT Population	14.2.5.3.2.1	
	Table	14.2.5.3.2.2	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q5 to Q16) Adaptation Domain Total Score	PP Population	14.2.5.3.2.1	
	Table	14.2.5.4.1.1	Summary of DHEQ (Section 2, Q17 to Q21) Social Impact Domain Total Score	mITT Population	14.2.5.4.1.1	
	Table	14.2.5.4.1.2	Summary of DHEQ (Section 2, Q17 to Q21) Social Impact Domain Total Score	PP Population	14.2.5.4.1.1	
	Table	14.2.5.4.2.1	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q17 to Q21) Social Impact Domain Total Score	mITT Population	14.2.5.4.2.1	
	Table	14.2.5.4.2.2	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q17 to Q21) Social Impact Domain Total Score	PP Population	14.2.5.4.2.1	
	Table	14.2.5.5.1.1	Summary of DHEQ (Section 2, Q22 to Q29) Emotional Impact Domain Total Score	mITT Population	14.2.5.5.1.1	
	Table	14.2.5.5.1.2	Summary of DHEQ (Section 2, Q22 to Q29) Emotional Impact Domain Total Score	PP Population	14.2.5.5.1.1	
	Table	14.2.5.5.2.1	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q22 to Q29) Emotional Impact Domain Total Score	mITT Population	14.2.5.5.2.1	

CSR Section	TLF	Number	Title	Population	Template	Topline
	Table	14.2.5.5.2.2	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q22 to Q29) Emotional Impact Domain Total Score	PP Population	14.2.5.5.2.1	
	Table	14.2.5.6.1.1	Summary of DHEQ (Section 2, Q30 to Q34) Identity Domain Total Score	mITT Population	14.2.5.6.1.1	
	Table	14.2.5.6.1.2	Summary of DHEQ (Section 2, Q30 to Q34) Identity Domain Total Score	PP Population	14.2.5.6.1.1	
	Table	14.2.5.6.2.1	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q30 to Q34) Identity Domain Total Score	mITT Population	14.2.5.6.2.1	
	Table	14.2.5.6.2.2	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q30 to Q34) Identity Domain Total Score	PP Population	14.2.5.6.2.1	
	Table	14.2.5.7.1.1	Summary of DHEQ (Section 2 Global Oral Health Score, Q35)	mITT Population	14.2.5.7.1.1	
	Table	14.2.5.7.1.2	Summary of DHEQ (Section 2 Global Oral Health Score, Q35)	PP Population	14.2.5.7.1.1	
	Table	14.2.5.7.2.1	Statistical Analysis of Change from Baseline in DHEQ (Section 2 Global Oral Health Score, Q35)	mITT Population	14.2.5.7.2.1	
	Table	14.2.5.7.2.2	Statistical Analysis of Change from Baseline in DHEQ (Section 2 Global Oral Health Score, Q35)	PP Population	14.2.5.7.2.1	
	Table	14.2.5.8.1.1	Summary of DHEQ (Section 2, Q36 to Q39) Effect on Life Overall score	mITT Population	14.2.5.8.1.1	
	Table	14.2.5.8.1.2	Summary of DHEQ (Section 2, Q36 to Q39) Effect on Life Overall score	PP Population	14.2.5.8.1.1	

CSR Section	TLF	Number	Title	Population	Template	Topline
	Table	14.2.5.8.2.1	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q36 to Q39) Effect on Life Overall score	mITT Population	14.2.5.8.2.1	
	Table	14.2.5.8.2.2	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q36 to Q39) Effect on Life Overall score	PP Population	14.2.5.8.2.1	
	Table	14.2.5.9.1	Summary of Satisfaction (%) with Treatment Numerical Rating Score (NRS)	mITT Population	14.2.5.9.1.1	
	Table	14.2.5.9.2	Summary of Satisfaction with Treatment Numerical Rating Score (NRS)	mITT Population	14.2.5.9.2.1	
	Figure	14.2.2.1.1	Mean (±SE) Schiff Sensitivity Score of the Two Test Teeth Over Time By Study Product	mITT Population	14.2.2.1.1	
	Figure	14.2.2.1.2	Mean (±SE) Schiff Sensitivity Score of the Two Test Teeth Over Time By Study Product	PP Population	14.2.2.1.1	
	Figure	14.2.2.2.1	Mean (±SE) Tactile Threshold (g) of the Two Test Teeth Over Time By Study Product	mITT Population	14.2.2.2.1	
	Figure	14.2.2.2.2	Mean (±SE) Tactile Threshold (g) of the Two Test Teeth Over Time By Study Product	PP Population	14.2.2.2.1	
	Figure	14.2.2.3.1	Mean (±SE) DHEQ (Section 2, Q1 to Q34) Total Score Over Time By Study Product	mITT Population	14.2.2.3.1	
	Figure	14.2.2.3.2	Mean (±SE) DHEQ (Section 2, Q1 to Q34) Total Score Over Time By Study Product	PP Population	14.2.2.3.1	
	Figure	14.2.2.4.1	Mean (±SE) DHEQ (Section 2, Q1 to Q4) Restriction Domain Total Score Over Time By Study Product	mITT Population	14.2.2.4.1	
	Figure	14.2.2.4.2	Mean (±SE) DHEQ (Section 2, Q1 to Q4) Restriction Domain Total Score Over Time By Study Product	PP Population	14.2.2.4.1	

CSR Section	TLF	Number	Title	Population	Template	Topline
	Figure	14.2.2.5.1	Mean (±SE) DHEQ (Section 2, Q5 to Q16) Adaptation Domain Total Score Over Time By Study Product	mITT Population	14.2.2.5.1	
	Figure	14.2.2.5.2	Mean (±SE) DHEQ (Section 2, Q5 to Q16) Adaptation Domain Total Score Over Time By Study Product	PP Population	14.2.2.5.1	
	Figure	14.2.2.6.1	Mean (±SE) DHEQ (Section 2, Q17 to Q21) Social Impact Domain Total Score Over Time By Study Product	mITT Population	14.2.2.6.1	
	Figure	14.2.2.6.2	Mean (±SE) DHEQ (Section 2, Q17 to Q21) Social Impact Domain Total Score Over Time By Study Product	PP Population	14.2.2.6.1	
	Figure	14.2.2.7.1	Mean (±SE) DHEQ (Section 2, Q22 to Q29) Emotional Impact Domain Total Score Over Time By Study Product	mITT Population	14.2.2.7.1	
	Figure	14.2.2.7.2	Mean (±SE) DHEQ (Section 2, Q22 to Q29) Emotional Impact Domain Total Score Over Time By Study Product	PP Population	14.2.2.7.1	
	Figure	14.2.2.8.1	Mean (±SE) DHEQ (Section 2, Q30 to Q34) Identity Domain Total Score Over Time By Study Product	mITT Population	14.2.2.8.1	
	Figure	14.2.2.8.2	Mean (±SE) DHEQ (Section 2, Q30 to Q34) Identity Domain Total Score Over Time By Study Product	PP Population	14.2.2.8.1	
	Figure	14.2.2.9.1	Mean (±SE) DHEQ (Section 2 Global Oral Health Score, Q35) Over Time By Study Product	mITT Population	14.2.2.9.1	
	Figure	14.2.2.9.2	Mean (±SE) DHEQ (Section 2 Global Oral Health Score, Q35) Over Time By Study Product	PP Population	14.2.2.9.1	
	Figure	14.2.2.10.1	Mean (±SE) DHEQ (Section 2, Q36 to Q39) Effect on Life Overall score Over Time By Study Product	mITT Population	14.2.2.10.1	
	Figure	14.2.2.10.2	Mean (±SE) DHEQ (Section 2, Q36 to Q39) Effect on Life Overall score Over Time By Study Product	PP Population	14.2.2.10.1	

CSR Section	TLF	Number	Title	Population	Template	Topline
	Figure	14.2.3.1	Mean (±SE) DHEQ (Section 1, Q7 to Q9) score Over Time By Question, Study Product	mITT Population	14.2.3.1	
	Figure	14.2.3.2	Mean (±SE) DHEQ (Section 1, Q7 to Q9) score Over Time By Question, Study Product	PP Population	14.2.3.1	
14.3 Safety Data Summary Tables and Figures						
14.3.1 Displays of Adverse Events						
	Table	14.3.1.1	Treatment Emergent Adverse Events by System Organ Class and Preferred Term	Safety Population	14.3.1.1	Yes
	Table	14.3.1.2	Treatment Emergent Adverse Events by Oral/Non-Oral and Preferred Term	Safety Population	14.3.1.2	
	Table	14.3.1.3	Treatment Related Treatment Emergent Adverse Events by System Organ Class and Preferred Term	Safety Population	14.3.1.1	
	Table	14.3.1.4	Treatment Related Treatment Emergent Adverse Events by Oral/Non-Oral and Preferred Term	Safety Population	14.3.1.2	
14.3.2 Listings of Deaths, Other Serious and Significant Adverse Events						
	Listing	14.3.2.1	Death	Safety Population	16.2.7.1	
	Listing	14.3.2.2	Non-fatal Serious Adverse Events	Safety Population	16.2.7.1	
	Listing	14.3.2.3	Treatment Emergent Adverse Events leading to Study or Product Discontinuation	Safety Population	16.2.7.1	
	Listing	14.3.2.4	Treatment Emergent Adverse Events Classified as Oral	Safety Population	16.2.7.1	
14.3.3 Narratives of Deaths, Other Serious and Certain Other Significant Adverse Events						

CSR Section	TLF	Number	Title	Population	Template	Topline
14.3.4 Other Observations Related to Safety and Abnormal Laboratory Values						
	Table	14.3.4.1	Summary of Oral Soft Tissue Examination	Safety Population	14.3.4.1	
APPENDIX						
16.1.6 Listing of Subjects Receiving Test Drug(s)/Investigational Product(s) from Specific Batches, where more than one batch was used						
	NA					
16.1.7 Randomization Scheme and Codes (Subject identification and treatment assigned)						
	Listing	16.1.7.1	Randomization Information	All Randomized Subjects	16.1.7.1	
	Listing	16.1.7.2	Kit List Allocation	All Randomized Subjects	16.1.7.2	
16.1.9 Documentation of Statistical Methods						
	Raw Output	16.1.9.1	Statistical Analysis of Change from Baseline in Schiff Sensitivity Score of the Two Test Teeth Over Time (Reference Table 14.2.2.2.1)	mITT Population	NA	Yes
	Raw Output	16.1.9.2	Statistical Analysis of Change from Baseline in Schiff Sensitivity Score of the Two Test Teeth Over Time (Reference Table 14.2.2.2.2)	PP Population	NA	
	Raw Output	16.1.9.3	Statistical Analysis of Change from Baseline in Tactile Threshold (g) of the Two Test Teeth Over Time (Reference Table 14.2.3.2.1)	mITT Population	NA	Yes
	Raw Output	16.1.9.4	Statistical Analysis of Change from Baseline in Tactile Threshold (g) of the Two Test Teeth Over Time (Reference Table 14.2.3.2.2)	PP Population	NA	

CSR Section	TLF	Number	Title	Population	Template	Topline
	Raw Output	16.1.9.5	Statistical Analysis of Change from Baseline in DHEQ (Section 1 Impact of Everyday Life, Q7 to Q9) (Reference Table 14.2.4.2.1)	mITT Population	NA	
	Raw Output	16.1.9.6	Statistical Analysis of Change from Baseline in DHEQ (Section 1 Impact of Everyday Life, Q7 to Q9) (Reference Table 14.2.4.2.2)	PP Population	NA	
	Raw Output	16.1.9.7	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q1 to Q34) Total Score Over Time (Reference Table 14.2.5.1.2.1)	mITT Population	NA	
	Raw Output	16.1.9.8	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q1 to Q34) Total Score Over Time (Reference Table 14.2.5.1.2.2)	PP Population	NA	
	Raw Output	16.1.9.9	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q1 to Q4) Restriction Domain Total Score (Reference Table 14.2.5.2.2.1)	mITT Population	NA	
	Raw Output	16.1.9.10	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q1 to Q4) Restriction Domain Total Score (Reference Table 14.2.5.2.2.2)	PP Population	NA	
	Raw Output	16.1.9.11	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q5 to Q16) Adaptation Domain Total Score (Reference Table 14.2.5.3.2.1)	mITT Population	NA	
	Raw Output	16.1.9.12	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q5 to Q16) Adaptation Domain Total Score (Reference Table 14.2.5.3.2.2)	PP Population	NA	

CSR Section	TLF	Number	Title	Population	Template	Topline
	Raw Output	16.1.9.13	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q17 to Q21) Social Impact Domain Total Score (Reference Table 14.2.5.4.2.1)	mITT Population	NA	
	Raw Output	16.1.9.14	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q17 to Q21) Social Impact Domain Total Score (Reference Table 14.2.5.4.2.2)	PP Population	NA	
	Raw Output	16.1.9.15	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q22 to Q29) Emotional Impact Domain Total Score (Reference Table 14.2.5.5.2.1)	mITT Population	NA	
	Raw Output	16.1.9.16	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q22 to Q29) Emotional Impact Domain Total Score (Reference Table 14.2.5.5.2.2)	PP Population	NA	
	Raw Output	16.1.9.17	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q30 to Q34) Identity Domain Total Score (Reference Table 14.2.5.6.2.1)	mITT Population	NA	
	Raw Output	16.1.9.18	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q30 to Q34) Identity Domain Total Score (Reference Table 14.2.5.6.2.2)	PP Population	NA	
	Raw Output	16.1.9.19	Statistical Analysis of Change from Baseline in DHEQ (Section 2 Global Oral Health Score, Q35) (Reference Table 14.2.5.7.2.1)	mITT Population	NA	
	Raw Output	16.1.9.20	Statistical Analysis of Change from Baseline in DHEQ (Section 2 Global Oral Health Score, Q35) (Reference Table 14.2.5.7.2.2)	PP Population	NA	

CSR Section	TLF	Number	Title	Population	Template	Topline
	Raw Output	16.1.9.21	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q36 to Q39) Effect on Life Overall score (Reference Table 14.2.5.8.2.1)	mITT Population	NA	
	Raw Output	16.1.9.22	Statistical Analysis of Change from Baseline in DHEQ (Section 2, Q36 to Q39) Effect on Life Overall score (Reference Table 14.2.5.8.2.2)	PP Population	NA	
16.2 Subject Data Listings						
16.2.1 Discontinued Subjects						
	Listing	16.2.1.1	Subject Disposition	All randomized subjects	16.2.1.1	
	Listing	16.2.1.2	Subject Disposition	Non-randomized subjects	16.2.1.2	
16.2.2 Protocol Deviations						
	Listing	16.2.2.1	Important Protocol Deviations	All randomized subjects	16.2.2.1	
	Listing	16.2.2.2	All Protocol Deviations	All randomized subjects	16.2.2.2	
16.2.3 Patients Excluded from the Efficacy Analysis						
	Listing	16.2.3.1	Exclusions from Analysis Populations	All randomized subjects	16.2.3.1	
16.2.4 Demographic Data						
	Listing	16.2.4.1	Demographic and Baseline Characteristics	All randomized subjects	16.2.4.1	

CSR Section	TLF	Number	Title	Population	Template	Topline
	Listing	16.2.4.2	Medical History and Current Medical Conditions	All randomized subjects	16.2.4.2	
	Listing	16.2.4.3	Prior medications	Safety Population	16.2.4.3	
	Listing	16.2.4.4	Concomitant medications and significant non-drug therapies taken during treatment	Safety Population	16.2.4.4	
16.2.5 Compliance and/or Drug Concentration Data (if available)						
	Listing	16.2.5.1	Brushing Compliance	All randomized subjects	16.2.5.1	
	Listing	16.2.5.2	Supervised Brushing	Safety Population	16.2.5.2	
16.2.6 Individual Efficacy Response Data						
	Listing	16.2.6.1	Individual Efficacy Data for Schiff Sensitivity Score (Screening and Baseline)	All Randomized Subjects	16.2.6.1	
	Listing	16.2.6.2	Individual Efficacy Data for Schiff Sensitivity Score of the Two Test Teeth	All Randomized Subjects	16.2.6.2	
	Listing	16.2.6.3	Individual Efficacy Data for Tactile Threshold (g) at Screening and Baseline	All Randomized Subjects	16.2.6.3	
	Listing	16.2.6.4	Individual Efficacy Data for Tactile Threshold (g) of the Two Test Teeth	All Randomized Subjects	16.2.6.4	
	Listing	16.2.6.5	Individual Efficacy Data for DHEQ Section 1	All Randomized Subjects	16.2.6.5	
	Listing	16.2.6.6.1	Individual Efficacy Data for DHEQ Section 2 (Restrictions Domain)	All Randomized Subjects	16.2.6.6.1	
	Listing	16.2.6.6.2	Individual Efficacy Data for DHEQ Section 2 (Adaptations Domain)	All Randomized Subjects	16.2.6.6.2	

CSR Section	TLF	Number	Title	Population	Template	Topline
	Listing	16.2.6.6.3	Individual Efficacy Data for DHEQ Section 2 (Social Impact Domain)	All Randomized Subjects	16.2.6.6.3	
	Listing	16.2.6.6.4	Individual Efficacy Data for DHEQ Section 2 (Emotional Impact Domain)	All Randomized Subjects	16.2.6.6.4	
	Listing	16.2.6.6.5	Individual Efficacy Data for DHEQ Section 2 (Identity Domain)	All Randomized Subjects	16.2.6.6.5	
	Listing	16.2.6.6.6	Individual Efficacy Data for DHEQ Section 2 (Total Score, Q1 to Q34)	All Randomized Subjects	16.2.6.6.6	
	Listing	16.2.6.6.7	Individual Efficacy Data for DHEQ Section 2 (Q35 to Q39)	All Randomized Subjects	16.2.6.6.7	
	Listing	16.2.6.7	Individual Efficacy Data for Numerical Rating Scale at Day 56	All Randomized Subjects	16.2.6.7	
16.2.7 Adverse Event Listings						
	Listing	16.2.7.1	Adverse Events	Safety Population	16.2.7.1	Yes
	Listing	16.2.7.2	Incidents	Safety Population	16.2.7.2	
16.2.8 Other Listings and Listing of Laboratory Measurements, when required by regulatory authorities (if applicable)						
	Listing	16.2.8.1	Oral Soft Tissue examination	Safety Population	16.2.8.1	
	Listing	16.2.8.2	Oral Hard Tissue examination	Safety Population	16.2.8.2	
16.4 Individual Subject Data Listings						
	NA					