3% PVM/MA + 5% $KNO_3$ Toothpaste
218220

# STATISTICAL ANALYSIS PLAN

## An 8-week, randomized, controlled, examiner-blind, proof of principle study investigating the ability of a 3% methyl vinyl ether/maleic anhydride co-polymer (PVM/MA) + 5% potassium nitrate ($KNO_3$) combination toothpaste to protect from dentine hypersensitivity

**Protocol Number:** 218220

**Phase:** Exploratory

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 | 23-MAR-2022 | Not applicable (N/A) |

## Table of Contents

## List of Tables

# Abbreviations

| Abbreviation | Term |
|---|---|
| AE | Adverse Event |
| ANCOVA | Analysis of Covariance |
| BDRM | Blinded Data Review Meeting |
| CI | Confidence Interval |
| COVID-19 | Coronavirus Disease of 2019 |
| CRS | Clinical Research Scientist |
| CSR | Clinical Study Report |
| DHEQ | Dentine Hypersensitivity Experience Questionnaire |
| EAR | Erosion/Abrasion/Recession |
| eCRF | Electronic Case Report Form |
| GSK CH | GlaxoSmithKline Consumer Healthcare |
| ICF | Informed Consent Form |
| KNO3 | Potassium Nitrate |
| MedDRA | Medical Dictionary for Regulatory Activities |
| MGI | Modified Gingival Index |
| mITT | Modified-Intent-to-Treat |
| NaF | Sodium Fluoride |
| NRS | Numeric Rating Scale |
| OHRQoL | Oral Health Related Quality of Life |
| OHT | Oral Hard Tissue |
| OST | Oral Soft Tissue |
| PoP | Proof of Principle |
| PP | Per-Protocol |
| ppm | parts per million |
| PT | Preferred Term |
| PVM/MA | Poly Vinyl Methyl ether/Maleic Anhydride |
| SAE | Serious Adverse Event |
| SAP | Statistical Analysis Plan |
| SD | Standard deviation |
| SE | Standard Error |
| SOC | System Organ Class |
| TEAE | Treatment Emergent Adverse Events |
| UPT | Urine Pregnancy Test |
| VAS | Visual Analog Scale |
| 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 218220.

# 1 Summary of Key Protocol Information

GlaxoSmithKline Consumer Healthcare (GSK CH) has developed a new combination toothpaste containing 3% poly vinyl methyl ether/maleic anhydride (PVM/MA) copolymer and 5% potassium nitrate ($KNO_3$). It is hypothesized that the combination of these two ingredients with different modes of action (PVM/MA: dentin tubule occlusion; $KNO_3$: nerve desensitization) will deliver superior protection for sensitive teeth from dentine hypersensitivity, compared to toothpastes containing either PVM/MA or $KNO_3$ alone. Toothpastes containing co-polymers such as PVM/MA are reported to alleviate tooth sensitivity. None of the studies reported to date investigated PVM/MA+$KNO_3$ formulations compared to the single ingredients. This proof of principle (PoP) clinical study will evaluate and compare the ability of the three products - a PVM/MA+$KNO_3$ combination toothpaste, a PVM/MA only toothpaste and a $KNO_3$ only toothpaste to provide sensitivity protection across an 8-week usage period. A regular fluoride toothpaste will be included as negative control.

## 1.1 Study Design

This will be a PoP, single center, 8-week, randomized, controlled, examiner blind, parallel design, stratified (by maximum Baseline Schiff sensitivity score of the two selected test teeth) clinical study in healthy subjects, investigating the ability of a 3% PVM/MA + 5% $KNO_3$ combination toothpaste to protect sensitive teeth from dentine hypersensitivity.

In line with widely recommended oral hygiene practice and typical consumer habit, study subjects will be requested to brush their teeth for one timed minute twice daily (morning and evening) with their assigned study toothpaste for the duration of the 8-week study period.

Tooth sensitivity will be assessed at Screening (Visit 1), Baseline (Day 0), Day 3 and Weeks 2, 4, and 8 using two independent stimulus-based (tactile and evaporative [air]) measures, in line with published recommendations for the design and conduct of sensitivity clinical studies. A single clinical examiner will assess both measures for the duration of the study for all study subjects. On completion of the Baseline assessments, the clinical examiner will select two ‘test teeth’ from those that qualified at Screening and Baseline, for assessment of tactile and evaporative (air) sensitivity at all subsequent visits. In addition, the remaining ‘eligible teeth’ identified as sensitive to both tactile and evaporative (air) stimuli at Screening will be assessed for evaporative (air) sensitivity only at Day 3 and Weeks 2, 4, and 8.

Oral Health Related Quality of Life (OHRQoL) will be evaluated using the validated Dentine Hypersensitivity Experience Questionnaire (DHEQ-15), completed by study subjects after 3days and 2-, 4- and 8-weeks product use. In addition, a Numeric Rating Scale (NRS) will be also used to explore changes in self-perceived discomfort associated to tooth sensitivity after 3 days and 2-, 4- and 8-weeks product use.

Safety and oral tolerability of the study products will be monitored over the 8-week usage period by review of reported Adverse Events (AEs).

Table 1-1 presents the schedule of activities.

3% PVM/MA + 5% $KNO_3$ Toothpaste
218220

**Table 1-1 Schedule of Activities**

| Procedure/Assessment | Screening | | Study Visits | | | | |
|---|---|---|---|---|---|---|---|
| | Visit 1 Day -28 to -14 | | Visit 2 **Baseline** Day 0 | Visit 3 **Day 3** (± 1 day) | Visit 4 **Week 2** Day 14 (± 1 day) | Visit 5 **Week 4** Day 28 (± 2 day) | Visit 6 **Week 8** Day 56 (± 2 day) |
| Informed Consent | X | Acclimatization Period (2 to 4 Weeks) | | | | | |
| Demographics | X | | | | | | |
| Medical History and Current/Prior Concomitant Medication/Treatment Review | X | | | | | | |
| Changes in Health and Medications/ Treatments | | | X | X | X | X | X |
| Urine Pregnancy Test (UPT)[1] | X | | | | | | X |
| Oral Soft Tissue (OST) Examination | 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 Tactile Sensitivity Assessment (Tactile Threshold) [2] | X | | X | | | | |

3% PVM/MA + 5% $KNO_3$ Toothpaste
218220

| Procedure/Assessment | Screening | | Study Visits | | | | |
|---|---|---|---|---|---|---|---|
| | Visit 1<br>Day -28<br>to -14 | | Visit 2<br>**Baseline**<br>Day 0 | Visit 3<br>**Day 3**<br>(± 1 day) | Visit 4<br>**Week 2**<br>Day 14<br>(± 1 day) | Visit 5<br>**Week 4**<br>Day 28<br>(± 2 day) | Visit 6<br>**Week 8**<br>Day 56<br>(± 2 day) |
| Qualifying Evaporative (Air) Sensitivity Assessment (Schiff sensitivity score)[3] | X | Acclimatization Period (2 to 4 Weeks) | X | | | | |
| Inclusion / Exclusion Criteria | X | | X | | | | |
| Subject Eligibility | X | | X | | | | |
| Dispense Acclimatization Toothpaste, Toothbrush, Timer and Diary | X | | | | | | |
| Supervised Brushing with Acclimatization Toothpaste | X | | | | | | |
| Return Acclimatization Toothpaste, Toothbrush and Diary[4] | | | X | | | | |
| Stratification/Randomization | | | X | | | | |
| Dispense Study Toothpaste, Toothbrush and Diary | | | X | | | | |
| Supervised Brushing with Study Toothpaste | | | X | X | X | X | |
| Return Study Toothpaste, Toothbrush and Diary[4] | | | | | | | X |
| Compliance Checks[5] | | | X | X | X | X | X |

| Procedure/Assessment | Screening | | Study Visits | | | | |
|---|---|---|---|---|---|---|---|
| | Visit 1<br>Day -28<br>to -14 | | Visit 2<br>**Baseline**<br>Day 0 | Visit 3<br>**Day 3**<br>(± 1 day) | Visit 4<br>**Week 2**<br>Day 14<br>(± 1 day) | Visit 5<br>**Week 4**<br>Day 28<br>(± 2 day) | Visit 6<br>**Week 8**<br>Day 56<br>(± 2 day) |
| Clinical Examiner Selects Two 'Test Teeth' (Eligible Subjects Only) | | Acclimatization Period (2 to 4 Weeks) | X | | | | |
| Tactile Sensitivity Assessment (Yeaple Probe): Two Test Teeth Only[2] | | | | X | X | X | X |
| Evaporative (Air) Sensitivity (Schiff sensitivity score): Two Test Teeth Only[3] | | | | X | X | X | X |
| Evaporative (Air) Sensitivity (Schiff sensitivity score): *All Remaining Eligible Teeth Identified at Screening*[3] | | | | X | X | X | X |
| DHEQ [6] | | | X[6] | X[6] | X[6] | X[6] | X[6] |
| NSR Self- Perceived Discomfort Questions | | | X | X | X | X | X |
| Study Conclusion | | | | | | | X |
| Monitor Adverse Events (AEs)[7] | | | X | X | X | X | X |

Footnotes:

1.Female subjects of child-bearing potential only.

2.**Visits 1 to 2:** maximum force 20 g (Screening and Baseline); **Visits 3 to 6:** maximum force 80 g.

3.Evaporative (air) assessment will follow tactile assessment, with minimum 5 minutes between last tactile assessment and first evaporative (air) assessment (to allow tooth recovery).

**Visit 1:** assess the evaporative (air) sensitivity of teeth with tactile threshold ≤ 20 g.

**Visit 2:** assess the evaporative (air) sensitivity of all eligible teeth identified at Screening.

**Visits 3 to 6:** assess the evaporative (air) sensitivity of the two test teeth first, then assess the evaporative (air) sensitivity of all other eligible teeth identified at Screening.

4.Subject will be required to bring their study supplies (minus timer) to every visit.
5.Perform visual check of returned study supplies, review diary and evaluate compliance.
**Visit 2:** check compliance with use of acclimatization toothpaste.
**Visits 3 to 6:** check compliance with use of study product.
**Visits 2 to 6:** check compliance with Lifestyle Guidelines/Medication requirements.
6.DHEQ must be completed before the NRS question is asked; DHEQ and NRS question must be completed prior to OST examination/clinical assessments.
DHEQ **Visit 2:** complete all questions
DHEQ **Visits 3 to 6:** complete Section 1 Q7 to Q9 and Section 2 all questions.
7.Record AEs from signing of informed consent until 5 days after last use of study product

## 1.2 Study Objectives

| Objectives | Endpoints |
|---|---|
| **Primary Objective** | **Primary Endpoint** |
| To characterise the sensitivity protection profile of an experimental 3% PVM/MA + 5% $KNO_3$ combination toothpaste, a 3% PVM/MA only toothpaste, a 5% $KNO_3$ and a regular fluoride toothpaste (negative control) over 8 weeks (with twice daily use). | At Day 0 (Baseline), Day 3 and Weeks 2, 4 and 8:<br>- Schiff sensitivity score<br>- Tactile threshold (grams [g])<br>- Number of sensitive teeth (Schiff sensitivity score ≥ 1) |
| **Secondary Objectives** | **Secondary Endpoints** |
| Efficacy | |
| To investigate the ability of an experimental 3% PVM/MA + 5% $KNO_3$ combination toothpaste to provide sensitivity protection, in response to an evaporative (air) stimulus (Schiff sensitivity score), compared to a 3% PVM/MA only toothpaste, a 5% $KNO_3$ only toothpaste and a regular fluoride toothpaste (negative control), after 3 days and 2, 4 and 8 weeks twice daily use. | At Day 3 and Weeks 2, 4 and 8:<br>Change from Baseline in Schiff sensitivity score |
| To investigate the ability of an experimental 3% PVM/MA + 5% $KNO_3$ combination toothpaste to provide sensitivity protection, in response to a tactile stimulus (tactile threshold), compared to a 3% PVM/MA only toothpaste, a 5% $KNO_3$ only toothpaste and regular fluoride toothpaste (negative control), after 3 days and 2, 4 and 8 weeks twice daily use. | At Day 3 and Weeks 2, 4 and 8:<br>Change from Baseline in tactile threshold (g) |
| To monitor Oral Health Related Quality of Life (OHRQoL), as measured by the Dentine Hypersensitivity Experience Questionnaire (DHEQ), after 3 days and 2, 4 and 8 weeks twice daily use of a 3% PVM/MA + 5% $KNO_3$ combination toothpaste, a 3% PVM/MA only toothpaste, a 5% $KNO_3$ only toothpaste and a regular fluoride toothpaste (negative control). | At Day 3 and Weeks 2, 4 and 8:<br>Change from Baseline in<br>- Responses to DHEQ Section 1, Questions 7-9<br>- Total Score; responses to DHEQ Section 2, Questions 1-15<br>- Restrictions, Adaptation, Social Impact, Emotional Impact and Identity Domains |
| To explore changes in self-perceived discomfort associated with tooth sensitivity, as measured by a numeric rating scale (NRS), after 3 days and 2, 4 and 8 weeks twice daily use of a 3% PVM/MA + 5% $KNO_3$ combination toothpaste, a 3% PVM/MA only toothpaste, a | At Baseline, Day 3 and Weeks 2, 4 and 8:<br>- NRS score<br>At Day 3 and Weeks 2, 4 and 8:<br>- Change from Baseline in NRS score |

| Objectives | Endpoints |
|---|---|
| 5% $KNO_3$ only toothpaste and a regular fluoride toothpaste (negative control). | |
| **Safety** | |
| To assess the safety and tolerability of study products with twice daily use for 8 weeks. | Treatment emergent adverse events |

No formal success criterion has been defined for this exploratory study; however, if the combination toothpaste provides greater sensitivity protection, it would be expected that the performance profiles (plots of Schiff sensitivity score, tactile threshold (g) and number of sensitive teeth) for the 3% PVM/MA + 5% $KNO_3$ toothpaste would show a consistent improvement in sensitivity with 8 weeks twice-daily use, directionally superior to the respective component formulations (PVM/MA alone and $KNO_3$ alone) and the negative control.

## 1.3 Treatments

Table 1-2 presents the acclimatization and study products.

**Table 1-2 Study Products**

| | Acclimatization Product | Test Product | Comparator 1 | Comparator 2 | Negative control |
|---|---|---|---|---|---|
| **Product Description** | Regular fluoride toothpaste | 3% PVM/MA + 5% $KNO_3$ combination toothpaste | 3% PVM/MA only toothpaste | 5% $KNO_3$ only toothpaste | Regular fluoride toothpaste |
| Fluoride Content | 1450 parts per million (ppm) fluoride as sodium fluoride (NaF) | 1450 ppm fluoride as NaF | 1450 ppm fluoride as NaF | 1450 ppm fluoride as NaF | 1450 ppm fluoride as NaF |
| Product Name | Colgate Cavity Protection | Not applicable (N/A) | N/A | N/A | Colgate Cavity Protection |
| Product Master Formulation Code (MFC) | Commercial Product | CCI | CCI | CCI | Commercial Product |
| Product Application | Subjects will dose the toothbrush provided with a strip of dentifrice (a full brush head) on each brushing occasion | | | | |
| Usage Instruction | Subjects will brush for one timed minute, twice daily (morning and evening); subjects will be permitted to rinse with water post-brushing. | Subjects will brush their two selected 'test teeth' first, followed by the whole mouth for one timed minute, twice daily (morning and evening); subjects will be permitted to rinse with water post-brushing. | | | |

Test Product, Comparator 1, Comparator 2, and Negative control will be considered as study products and analyzed as per this document.

### 1.4 Sample Size Calculation

No formal sample size has been produced for this PoP clinical study to investigate changes in sensitivity measures (Schiff sensitivity score, tactile threshold, and number of sensitive teeth) over time with twice-daily use of a novel combination toothpaste. Based on previous, similar GSK CH studies evaluating the sensitivity protection provided by daily-use toothpastes, approximately 30 evaluable subjects per product group is considered sufficient to provide reliable estimates of performance for the purposes of this study and to aid in the design of future clinical studies. Approximately 120 subjects will be randomized to study product.

From a previous, similar GSK CH study (GSK CH Clinical Study 209723, 2020), change in Schiff sensitivity score at Week 8 had standard deviation (SD) of 0.7 units and the degree of variability in the test and control groups remained roughly consistent with each other over time. A similar trend was observed for the tactile threshold and number of sensitive teeth endpoints.

A sample size of 30 evaluable subjects per product group is expected to provide 95% Confidence Intervals (CIs) with a width of ±0.261 units for the Schiff sensitivity score. This level of precision is considered sufficient for the purposes of this study. Approximately 120 subjects will be randomized to study treatment.

## 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 including any external data reconciliation 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 Day 0 (Visit 2) pre-brushing 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

Subgroups are not defined for this trial.

Subjects will be stratified (by 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 case of mis-stratification, the actual stratification based on the baseline Schiff scores will be used in the efficacy analyses as a factor.

## 3.3 Centers Pools

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

## 3.4 Timepoints and Visit Windows

The time points and visits for this study are defined in Table 1-1 "Schedule of Activities". Any deviation from the study schedule will 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) Population.

# 4 Data Analysis

Data analysis will be performed by CCI [redacted]. Statistical analysis software SAS (Studio) version 9.4 or higher will be used.

Prior to database closure a BDRM will be conducted at which various aspects of the trial will be discussed and necessary actions, including exclusions from the Safety, modified Intent-to-Treat (mITT) and PP Populations.

One aspect that will be considered prior to or during BDRM is the assessment of the number of subjects who have dropped or discontinued from the study due to pandemic related events (e.g.,

Coronavirus Disease of 2019 [COVID-19]) and the potential need of a sensitivity analysis. Any major changes to planned analyses will need an amendment to SAP.

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

## 4.1 Populations for Analysis

### 4.1.1 Subject Disposition

Subject disposition will be presented in Table 14.1.1.

The number of subjects screened, subjects not randomized, and subjects enrolled will be presented for all screened subjects in Table 14.1.1. Table 14.1.1 will also display the number and percentage of screen failure subjects (subjects not randomized) with reasons why subjects are not randomized, including percentage of subjects not randomized due to COVID-19 pandemic. Percentages for screen failure subjects will be based on the total number of subjects screened.

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 will be presented.

The number and percentage of subjects randomized, who complete the study and who discontinue the study broken down by reason for discontinuation including percentage of subjects discontinued/withdrew from study due to COVID-19 pandemic, by study product and overall will also be displayed. The percentages will be based on the total 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, and race), screening date, study product start date and time, last study product administration 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 minus start date of study product use) + 1]), duration (in days) of study product usage (defined as: [(date of last study product use minus date of first study product use)+1]), subject discontinued/withdrew from study due to COVID-19 pandemic and the primary reason for withdrawal will be listed (Listing 16.2.1.1) by study product group.

Subject disposition information will be listed for non-randomized subjects (Listing 16.2.1.2), displaying subject number, demographic information (age, sex, and race), screening date, reason for screen failure, any further details of reason for screen failure and discontinuation status due to COVID-19 pandemic.

### 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 categorized. Subjects with important protocol deviations liable to influence the efficacy outcomes will be excluded from the PP Population. Subjects may also be identified as having important protocol deviations not leading to exclusion from the PP Population.

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

- Consent procedures
- Inclusion/Exclusion criteria
- Non-compliance with product administration
- Study procedures
- Inadmissible concomitant medication

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

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

All protocol deviations collected on the protocol deviation electronic Case Report Form (eCRF) will be listed in Listing 16.2.2.2 by study product for all randomized subjects. 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 complete at least one use of study product.<br>Any subject who receives a randomization number will be considered to have been randomized.<br>This population will be based on the study product the subject actually received. | Safety Analysis |
| mITT | Comprise all randomized subjects who complete at least one use of study product and have at least one post- | Demographic and Baseline Characteristics, Efficacy Analysis |

| Population | Definition / Criteria | Analyses Evaluated |
|---|---|---|
| | baseline clinical performance assessment (Schiff sensitivity assessment or Tactile sensitivity assessment).<br>Any subject who receives a randomization number will be considered to have been randomized.<br>This population will be based on the study product to which the subject was randomized. | |
| PP | Comprise all randomized subjects who do not have any protocol deviations that could confound the interpretation of analyses conducted on mITT.<br>Protocol deviations that would exclude subjects from the PP Population are defined in Section 4.1.2.<br>This population will be based on the study product to which the subject was randomized. | Efficacy Analysis |

NOTES :

- Please refer to Attachment 1: List of Data Displays which details the population to be used for each display being generated.

The primary population for assessment of efficacy will be the mITT Population. A PP analysis will be performed on the primary and secondary variables (Schiff score and Tactile threshold) if there is more than 10% difference in the number of subjects between the PP and mITT Population. A decision will be made to perform PP analysis after the BDRM but prior to study unblinding (release of the randomization codes).

The numbers of subjects included in each of the analysis populations will be presented (Table 14.1.1). Exclusion from analysis populations will be listed in Listing 16.2.3.1.

## 4.2 Subject Demographics and Other Baseline Characteristics

### 4.2.1 Demographic Characteristics

Descriptive statistics (number of subjects [n], mean, SD, median, minimum, and maximum for continuous variables and frequency count [n] and percentage [%] of subjects for categorical variables) will be presented for demographic variables and baseline characteristics by study product and overall. These variables include age, gender, race, and baseline Schiff stratification score, and will be presented for Safety and mITT Populations (Table 14.1.3.1 and Table 14.1.3.2, respectively).

Demographic and baseline characteristics information will be listed (Listing 16.2.4.1) for all randomized subjects by study product.

### 4.2.2 General Medical History

General medical history and current medical conditions will be listed in Listing 16.2.4.2 for all randomized subjects, with start date and end date or ongoing at the start of study drug.

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

Randomization details will be listed, including the randomization number, stratification group, planned study product, actual study product and the randomization date (Listing 16.1.7.1).

The study product kit allocations will be listed (Listing 16.1.7.2), including kit number and study product information.

### 4.3.1 Study Product Compliance and Exposure

Study product compliance data will be summarized for the mITT Population and will be assessed by number of brushings

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

Number of brushings is defined as: [(date of Visit N – date of Visit 2) multiplied by 2 – number of missing brushings + number of additional brushings].

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

Details about study product supervised brushings will be listed (Listing 16.2.5.2) for all randomized subjects by study product.

### 4.3.2 Prior and Concomitant Medication

Any medications, treatments or vaccine (including over-the-counter or prescription medicines, vitamins, and/or herbal supplements) taken during the study, from signing the informed consent, must be recorded in the CRF with indication, reason for use, unit dose, daily dose, and start and stop dates of administration. All subjects will be questioned about medications/treatments at each site visit.

Medication/treatments taken within 30 days of signing the Informed Consent Form (ICF) will be documented as a prior medication/treatment. Medications/treatments taken after signing the ICF will be documented as concomitant medication/treatments.

Prior medications will be listed by subject and study product group, with drug name, World Health Organization Drug Dictionary (WHODD) drug synonym, dose, dose form, frequency, route, start date, and end date (Listing 16.2.4.3) for all screened subjects. Concomitant

medications and significant non-drug therapies will be listed similarly (Listing 16.2.4.4) for all randomized subjects (Listing 16.2.4.5) for non-randomized subjects.

Unknown dates will not be imputed. If the stop date is unknown, or incomplete, and the medication cannot be considered as stopped prior to the date of signing the ICF then the medication will be considered as a concomitant medication (unless partial start or stop dates indicate differently).

## 4.4 Analysis of Efficacy

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

### 4.4.1 Primary Efficacy Endpoint

#### 4.4.1.1 Primary Efficacy Endpoint Definition

The primary efficacy variables are Schiff sensitivity score, tactile threshold (g) , and the number of sensitive teeth (defined as number of teeth with Schiff sensitivity score ≥ 1) at Day 0 (Baseline), Day 3, Weeks 2, 4, and 8.

Schiff sensitivity score and tactile threshold will be derived as the average score of the two test teeth. In addition, for tactile threshold (g), the tooth recorded as >20 g (for screening and baseline) or >80 g (for post baseline) will be rounded up to the next increment of 10 g for the calculation of average tactile threshold (g).

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.

Similar to Schiff sensitivity score, other primary efficacy endpoints will also be summarized in Table 14.2.2.2.1 and Table 14.2.2.3.1 (for tactile threshold (g) and number of sensitive teeth, respectively) and in Figure 14.2.2.2.1 and Figure 14.2.2.3.1 (for tactile threshold (g) and the number of sensitive teeth, respectively) for subjects in mITT Population.

Individual Schiff sensitivity score and tactile threshold (g) 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, respectively, for all randomized subjects. The number of sensitive teeth will be listed by subject, visit and study product group in Listing 16.2.6.3 for all randomized subjects.

#### 4.4.1.2 Statistical Hypothesis, Model, and Method of Analysis

The analysis of primary efficacy endpoints will descriptively and visually present the performance of the study products over time. No formal statistical analysis is planned for assessment of primary efficacy endpoints.

#### 4.4.1.3 Supportive Analyses

If there is more than 10% difference in the overall number of subjects between PP and mITT Populations, a summary of the Schiff Sensitivity Score, tactile threshold (g) and number of sensitive teeth will be presented for the PP Population in Table 14.2.2.1.2, Table 14.2.2.2.2, and Table 14.2.2.3.2, respectively. In addition, Schiff sensitivity score (Figure 14.2.2.1.2), tactile threshold (g) (Figure 14.2.2.2.2) and number of sensitive teeth (Figure 14.2.2.3.2) at each time point will be plotted by study product in for all subjects in PP Population.

### 4.4.2 Secondary Efficacy Variables

#### 4.4.2.1 Analysis of Secondary Objectives

##### 4.4.2.1.1 Secondary Efficacy Endpoint 1 Definition

The first secondary endpoint is change from baseline in Schiff sensitivity score at Day 3, Weeks 2, 4, and 8. Change from baseline will be derived for the individual teeth first before calculating the average change for the two test teeth.

Descriptive statistics (n, mean, SD, Standard Error [SE], median, minimum, and maximum) will be presented for change from baseline in Schiff sensitivity score at each assessment time point in Table 14.2.2.1.1 for all subjects in mITT Population by study product. Figure 14.2.2.1.1 presents raw mean (± SE) at each timepoint for mITT Population.

##### 4.4.2.1.2 Statistical Hypothesis, Model and Method of Analysis

Study product differences will be tested under the null hypothesis:

- $H_0$: there is no treatment difference
- $H_1$: there is a treatment difference

The following study product comparisons will be analyzed:

- Test product versus negative control
- Test product versus comparator 1
- Test product versus comparator 2

Change in Schiff sensitivity score at Day 3, Weeks 2, 4, and 8 will be analyzed using an Analysis of Covariance (ANCOVA) model which will include study product as a factor and baseline Schiff sensitivity score as a covariate. Since the baseline Schiff sensitivity score will be included as a covariate, the baseline Schiff stratification value will not be included in the model.

Using the above model, adjusted mean change from baseline, along with 95% CIs will be reported by study product group. P-values testing for non-zero change from baseline will be presented for both study product groups. Mean difference between study product groups, 95% CIs and p-values will be provided for Schiff sensitivity score in Table 14.2.2.4.1. Significance

testing will be conducted at the two-sided 5% significance level; no adjustment for multiple comparisons will be made.

The assumption of normality and homogeneity of variance in the ANCOVA model will be investigated, and if violated, an appropriate data transformation or non-parametric method, for example, the van Elteren test, adjusting for baseline Schiff stratification, will be performed.

### 4.4.2.2 Secondary Efficacy Variable 2

#### 4.4.2.2.1 Secondary Efficacy Endpoint 2 Definition

The second secondary endpoint is change from baseline in Tactile threshold (g) at Day 3, Weeks 2, 4, and 8. Change from Baseline will be derived for the individual teeth first before calculating the average change for the two test teeth. The tooth recorded as >20 g (for screening and baseline) or >80 g (for post baseline) will be rounded up to the next increment of 10 g for the calculation of change from baseline in tactile threshold (g).

Descriptive statistics (n, mean, SD, SE, median, minimum, and maximum) will be presented for change from baseline in Tactile threshold (g) at each assessment time point in Table 14.2.2.2.1 for all subjects in mITT Population by study product. Figure 14.2.2.2.1 presents raw mean (± SE) at each timepoint for mITT Population.

#### 4.4.2.2.2 Statistical Hypothesis, Model and Method of Analysis

Study product differences will be tested under the null hypothesis:

- $H_0$: there is no treatment difference versus the alternate hypothesis
- $H_1$: there is a treatment difference

The following study product comparisons will be analyzed:

- Test product versus negative control
- Test product versus comparator 1
- Test product versus comparator 2

Change from baseline in tactile threshold (g) will be analyzed at Day 3, Weeks 2, 4, and 8 using an ANCOVA model with study product and baseline Schiff stratification included as factors and baseline tactile threshold (g) included as a covariate.

Using the above model, adjusted mean change from baseline, along with 95% CIs will be reported by study product group. The adjusted means will be derived using weighted model effects for the baseline Schiff stratification which are proportional to the split between strata observed in the data. P-values testing for non-zero change from baseline will be presented for both study product groups. Mean difference between study product groups, 95% CIs and p-values will be provided for tactile threshold (g) in Table 14.2.2.4.2. Significance testing will be conducted at the two-sided 5% significance level; no adjustment for multiple comparisons will be made.

The assumption of normality and homogeneity of variance in the ANCOVA model will be investigated, and if violated, an appropriate data transformation or non-parametric method, for example, the van Elteren test, adjusting for baseline Schiff stratification, will be performed.

#### 4.4.2.3 Secondary Efficacy Variable 3

##### 4.4.2.3.1 Secondary Efficacy Endpoint 3 Definition

The third secondary endpoint is change from baseline in DHEQ at Day 3, Weeks 2, 4, and 8.

The following DHEQ-15 endpoints will be reported:

- Responses to Questions 1 to 6, DHEQ Section 1 at baseline (as separate questions);
- Responses to Questions 7, 8 and 9, DHEQ Section 1 (as separate questions);
- Total Score for Questions 1 to 15, DHEQ Section 2;
- Restrictions Domain (total score for Questions 1 to 3, DHEQ Section 2);
- Adaptation Domain (total score for Questions 4 to 6, DHEQ Section 2);
- Social Impact Domain (total score for Questions 7 to 9, DHEQ Section 2);
- Emotional Impact Domain (total score for Questions 10 to 12, DHEQ Section 2);
- Identity Domain (total score for Questions 13 to 15, DHEQ Section 2);
- Change from Baseline at Day 3, and Weeks 2, 4, and 8 for each DHEQ endpoint.

Descriptive statistics (n, mean, SD, SE, median, minimum, and maximum) will be presented for observed scores and change from baseline for each DHEQ endpoint by study product group in Table 14.2.3.1 (For DHEQ Section 1, Q1 to Q6), Table 14.2.3.2 (for DHEQ Section 1, Q7 to Q9) and Table 14.2.3.3 (for DHEQ Section 2) for all subjects in mITT Population. Individual DHEQ scores will be listed in Listing 16.2.6.4 (for DHEQ Section 1) and Listing 16.2.6.5 (for DHEQ Section 2) for all randomized subjects.

##### 4.4.2.3.2 Statistical Hypothesis, Model and Method of Analysis

No formal statistical analysis is planned for assessment of DHEQ endpoints.

#### 4.4.2.4 Secondary Efficacy Variable 4

##### 4.4.2.4.1 Secondary Efficacy Endpoint 4 Definition

The fourth secondary endpoint is changes in self-perceived discomfort associated with tooth sensitivity, as measured by a NRS, at Day 3 and Weeks 2, 4, and 8.

The 11-item NRS is a segmented numeric version of the Visual Analog Scale (VAS) in which a respondent selects the number (0 to 10) that best reflects the intensity of the discomfort caused by their sensitivity. Similar to the VAS, the NRS is anchored by terms describing discomfort extremes and ranges from 0 = no discomfort to 10 = worst discomfort imaginable.

Descriptive statistics (n, mean, SD, SE, median, minimum, and maximum) will be presented for observed NRS and change from baseline in NRS at each assessment time point by study product group in Table 14.2.4.1 for all subjects in mITT Population. Individual NRS data will be listed in Listing 16.2.6.6 for all randomized subjects. In addition, raw mean (± SE) of NRS will be plotted over time (Figure 14.2.4) for mITT Population.

#### 4.4.2.4.2 Statistical Hypothesis, Model and Method of Analysis

No formal statistical analysis is planned for assessment of NRS.

### 4.4.3 Pharmacokinetic (Secondary)

NA.

### 4.4.4 Handling of Missing Values/Censoring/Discontinuations

Subjects who withdraw from the study early will be included in the statistical analysis up to the point of withdrawal. Subjects who withdraw will not be replaced. Data will not be imputed in the case of dropouts or missing data.

## 4.5 Analysis of Safety

All safety data will be reported for the Safety Population as per actual study product received. The safety profile of the study products will be assessed with respect to AEs, OST and OHT findings

### 4.5.1 Adverse Events and Serious Adverse Events

All AEs will be reviewed by the Clinical Research Scientist (CRS) or Designee prior to database lock and unblinding and will be coded to a system organ class (SOC) and preferred term (PT) using the Medical Dictionary for Regulatory Activities (MedDRA). During this review stage, AEs will be further categorized as oral or non-oral.

Treatment emergent adverse events (TEAEs) are defined as AEs that occur on or after the first study product use at the Baseline visit (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 application will be considered as non-treatment emergent.

The following AE tables and listings will be produced, presented by study product group and overall:

- 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).
- Table of AEs related to COVID-19 by SOC and PT (Table 14.3.1.5).

- Listing of all AEs (Listing 16.2.7.1 for all randomized subjects; Listing 16.2.7.2 for non-randomized subjects).
- Listing of all AEs related to COVID-19 (Listing 16.2.7.3 for all screened subjects)
- 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 product 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. In addition, in case of more than 5 SAEs, a table with SAEs by SOC and PT 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

An OST examination will be conducted for each subject at every visit prior to any clinical assessments. The examination will be accomplished by direct observation and palpation, using retraction aids as appropriate, and will include examination of the labial mucosa (including lips), buccal mucosa, and 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 with details of any abnormalities. Any abnormality or worsening of a preexisting condition observed by the clinical examiner or reported by the subject from the OST examination carried out 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 all randomized subjects.

#### 4.5.2.2 OHT Examination

The OHT examination will be accomplished by direct observation, using retraction aids as appropriate and will identify any grossly carious lesions or signs of erosive wear, enamel irregularities, tooth fracture, gross decay, decalcification, and faulty restorations.

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. Observations will be listed as either absent or present, and conditions noted as present will be described in

the eCRF. Any change observed by the clinical examiner or reported by the subject from the OHT examination carried out at Screening will be recorded as an AE.

OHT examination will be listed (Listing 16.2.8.2) for all randomized subjects.

### 4.6 Analysis of Other Variables

NA

## 5 Changes to the Protocol Defined Statistical Analysis Plan

There were no changes or deviations to the originally planned statistical analysis specified in the protocol version 2.0 (Dated: 25/JAN/2022).

# 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 | Table 14.1.1 | Yes |
| | Table | 14.1.2 | Incidence of Important Protocol Deviations | All Randomized Subjects | Table 14.1.2 | |
| | Table | 14.1.3.1 | Demographic Characteristics | Safety Population | Table 14.1.3.1 | Yes |
| | Table | 14.1.3.2 | Demographic Characteristics | mITT Population | Table 14.1.3.1 | |
| 14.2 Efficacy Data Summary Tables and Figures | | | | | | |
| | Table | 14.2.1 | Summary of Brushing Compliance | mITT Population | Table 14.2.1 | |
| | Table | 14.2.2.1.1 | Summary of Schiff Sensitivity Score | mITT Population | Table 14.2.2.1.1 | Yes |
| | Table | 14.2.2.1.2 | Summary of Schiff Sensitivity Score | PP Population | Table 14.2.2.1.1 | |
| | Table | 14.2.2.2.1 | Summary of Tactile Threshold (g) | mITT Population | Table 14.2.2.2.1 | Yes |
| | Table | 14.2.2.2.2 | Summary of Tactile Threshold (g) | PP Population | Table 14.2.2.2.1 | |
| | Table | 14.2.2.3.1 | Summary of Number of Sensitive Teeth | mITT Population | Table 14.2.2.3.1 | |

| CSR Section | TLF | Number | Title | Population | Template | Topline |
|---|---|---|---|---|---|---|
| | Table | 14.2.2.3.2 | Summary of Number of Sensitive Teeth | PP Population | Table 14.2.2.3.1 | |
| | Table | 14.2.2.4.1 | Statistical Analysis of Change from Baseline in Schiff Sensitivity Score Over Time | mITT Population | Table 14.2.2.4.1 | Yes |
| | Table | 14.2.2.4.2 | Statistical Analysis of Change from Baseline in Tactile Threshold (g) Over Time | mITT Population | Table 14.2.2.4.2 | Yes |
| | Table | 14.2.3.1 | Summary of Subject Response to the DHEQ Section 1 at Baseline (Q1 to Q6) | mITT Population | Table 14.2.3.1 | |
| | Table | 14.2.3.2 | Summary of Subject Response to the DHEQ Section 1 (Q7 to Q9) | mITT Population | Table 14.2.3.2 | |
| | Table | 14.2.3.3 | Summary of Subject Response to the DHEQ Section 2 | mITT Population | Table 14.2.3.3 | |
| | Table | 14.2.4.1 | Summary of Numerical Rating Scale | mITT Population | Table 14.2.4.1 | |
| | Figure | 14.2.2.1.1 | Schiff Sensitivity Score over time | mITT Population | Figure 14.2.2.1.1 | |
| | Figure | 14.2.2.1.2 | Schiff Sensitivity Score over time | PP Population | Figure 14.2.2.1.1 | |
| | Figure | 14.2.2.2.1 | Tactile Threshold (g) Over time | mITT Population | Figure 14.2.2.2.1 | |

| CSR Section | TLF | Number | Title | Population | Template | Topline |
|---|---|---|---|---|---|---|
| | Figure | 14.2.2.2.2 | Tactile Threshold (g) Over time | PP Population | Figure 14.2.2.2.1 | |
| | Figure | 14.2.2.3.1 | Number of Sensitive Teeth over time | mITT Population | Figure 14.2.2.3.1 | |
| | Figure | 14.2.2.3.2 | Number of Sensitive Teeth over time | PP Population | Figure 14.2.2.3.1 | |
| | Figure | 14.2.4 | Numerical Rating Scale over time | mITT Population | Figure 14.2.4 | |
| 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 | Table 14.3.1.1 | |
| | Table | 14.3.1.2 | Treatment Emergent Adverse Events by Oral/Non-Oral and Preferred Term | Safety Population | Table 14.3.1.2 | |
| | Table | 14.3.1.3 | Treatment Related Treatment Emergent Adverse Events by System Organ Class and Preferred Term | Safety Population | Table 14.3.1.1 | |
| | Table | 14.3.1.4 | Treatment Related Treatment Emergent | Safety Population | Table 14.3.1.2 | |

| CSR Section | TLF | Number | Title | Population | Template | Topline |
|---|---|---|---|---|---|---|
| | | | Adverse Events by Oral/Non-Oral and Preferred Term | | | |
| | Table | 14.3.1.5 | Adverse Events Related to COVID-19 | Safety Population | Table 14.3.1.5 | |
| 14.3.2 Listings of Deaths, Other Serious and Significant Adverse Events | | | | | | |
| | Listing | 14.3.2.1 | Death | Safety Population | Listing 16.2.7.1 | |
| | Listing | 14.3.2.2 | Non-fatal Serious Adverse Events | Safety Population | Listing 16.2.7.1 | |
| | Listing | 14.3.2.3 | Treatment Emergent Adverse Events leading to Study or Product Discontinuation | Safety Population | Listing 16.2.7.1 | |
| | Listing | 14.3.2.4 | Treatment Emergent Adverse Events Classified as Oral | Safety Population | Listing 16.2.7.1 | |
| 14.3.3 Narratives of Deaths, Other Serious and Certain Other Significant Adverse Events | | | | | | |
| | NA | | | | | |
| 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 | Table 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 | | | | | |

| CSR Section | TLF | Number | Title | Population | Template | Topline |
|---|---|---|---|---|---|---|
| 16.1.7 Randomization Scheme and Codes (Subject identification and treatment assigned) | | | | | | |
| | Listing | 16.1.7.1 | Randomization Information | All Randomized Subjects | Listing 16.1.7.1 | |
| | Listing | 16.1.7.2 | Kit List Allocation | All Randomized Subjects | Listing 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 Over Time (Reference Table 14.2.2.4.1) | mITT Population | NA | |
| | Raw Output | 16.1.9.2 | Statistical Analysis of Change from Baseline in Tactile Threshold (g) Over Time (Reference Table 14.2.2.4.2) | mITT Population | NA | |
| 16.2 Subject Data Listings | | | | | | |
| 16.2.1 Discontinued Subjects | | | | | | |
| | Listing | 16.2.1.1 | Subject Disposition | All Randomized Subjects | Listing 16.2.1.1 | |
| | Listing | 16.2.1.2 | Subject Disposition | Non-randomized Subjects | Listing 16.2.1.2 | |
| 16.2.2 Protocol Deviations | | | | | | |

| CSR Section | TLF | Number | Title | Population | Template | Topline |
|---|---|---|---|---|---|---|
| | Listing | 16.2.2.1 | Important Protocol Deviations | All Randomized Subjects | Listing 16.2.2.1 | |
| | Listing | 16.2.2.2 | All Protocol Deviations | All Randomized Subjects | Listing 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 | Listing 16.2.3.1 | |
| 16.2.4 Demographic Data | | | | | | |
| | Listing | 16.2.4.1 | Demographic and Baseline Characteristics | All Randomized Subjects | Listing 16.2.4.1 | |
| | Listing | 16.2.4.2 | Medical History and Current Medical Conditions | All Randomized Subjects | Listing 16.2.4.2 | |
| | Listing | 16.2.4.3 | Prior medications | All Screened Subjects | Listing 16.2.4.3 | |
| | Listing | 16.2.4.4 | Concomitant Medications and Significant Non-drug Therapies | All Randomized Subjects | Listing 16.2.4.4 | |
| | Listing | 16.2.4.5 | Concomitant Medications and Significant Non-drug Therapies | Non-randomized Subjects | Listing 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 | Listing 16.2.5.1 | |

| CSR Section | TLF | Number | Title | Population | Template | Topline |
|---|---|---|---|---|---|---|
| | Listing | 16.2.5.2 | Supervised Brushing | All Randomized Subjects | Listing 16.2.5.2 | |
| 16.2.6 Individual Efficacy Response Data | | | | | | |
| | Listing | 16.2.6.1 | Individual Efficacy Data for Schiff Sensitivity Score for the Two Test Teeth | All Randomized Subjects | Listing 16.2.6.1 | |
| | Listing | 16.2.6.2 | Individual Efficacy Data for Tactile Threshold (g) for the Two Test Teeth | All Randomized Subjects | Listing 16.2.6.2 | |
| | Listing | 16.2.6.3 | Individual Efficacy Data for Number of Sensitive Teeth (Schiff Sensitivity Score >= 1) | All Randomized Subjects | Listing 16.2.6.3 | |
| | Listing | 16.2.6.4 | DHEQ Section 1 | All Randomized Subjects | Listing 16.2.6.4 | |
| | Listing | 16.2.6.5 | DHEQ Section 2 | All Randomized Subjects | Listing 16.2.6.5 | |
| | Listing | 16.2.6.6 | Individual Efficacy Data for Numerical Rating Scale | All Randomized Subjects | Listing 16.2.6.6 | |
| 16.2.7 Adverse Event Listings | | | | | | |
| | Listing | 16.2.7.1 | All Adverse Events | All Randomized Subjects | Listing 16.2.7.1 | Yes |
| | Listing | 16.2.7.2 | All Adverse Events | Non-randomized Subjects | Listing 16.2.7.1 | |

| CSR Section | TLF | Number | Title | Population | Template | Topline |
|---|---|---|---|---|---|---|
| | | | | | | |
| | Listing | 16.2.7.3 | Adverse Events Related to COVID-19 | All Screened subjects | Listing 16.2.7.1 | |
| 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 | All Randomized Subjects | Listing 16.2.8.1 | |
| | Listing | 16.2.8.2 | Oral Hard Tissue Examination | All Randomized Subjects | Listing 16.2.8.2 | |
| 16.4 Individual Subject Data Listings | | | | | | |
| | NA | | | | | |