Sodium-calcium mixed partial salt of poly (methylvinylether/maleic acid) and carboxymethylcellulose
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gsk GlaxoSmithKline
Consumer Healthcare

STATISTICAL REPORTING AND ANALYSIS PLAN

A RANDOMIZED, SINGLE-BLIND, CLINICAL STUDY TO ASSESS FOOD OCCLUSION EFFICACY OF A MARKETED DENTURE ADHESIVE IN HEALTHY, EDENTULOUS SUBJECTS

Protocol Number: 209649

Phase: 4

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Document History

Document	Version Date	Summary of Changes (New analysis or Change in planned analysis)
Original Analysis Plan Text	28-Jan-2019	Not applicable (N/A)

Amendments incorporate all revisions to date.

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Abbreviation

Abbreviation	Term
AE	Adverse Event
ANOVA	Analysis of Variance
BDRM	Blinded Data Review Meeting
CI	Confidence Interval
CRF	Case Report Form
CV	Coefficient of Variation
gm	gram
GSK CH	GlaxoSmithKline Consumer Healthcare
MedDRA	Medical Dictionary for Regulatory Activities
mg	milligram
MITT	Modified Intent-To-Treat
N/A	Not Applicable
OST	Oral Soft Tissue
PASS	Power Analysis and Sample Size
PP	Per-Protocol
PT	Preferred Term
SD	Standard Deviation
SE	Standard Error
SOC	System Organ Class
TEAE	Treatment Emergent Adverse Event

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The purpose of this Statistical Reporting and Analysis Plan is to describe the planned analyses and outputs to be included in the Clinical Study Report for Protocol 209649 version 2.0 dated 19-Dec-2018.

1 Summary of Key Protocol Information

This study is designed to investigate the effectiveness of a marketed denture adhesive, dispensed through a precision nozzle to prevent the ingress of peanut particles under dentures, in a food occlusion model. The study will compare COREGA Maximo Sellado/Selamento with a precision nozzle versus no adhesive using the methodology that was developed under study 208397.

This study will compare the efficacy of a marketed denture adhesive against use of no adhesive. No adhesive has been chosen as a control group to provide a continual reference point to allow interpretation of results and to facilitate comparison of the results from this study with previous work, and is representative of a significant number of denture wearers who currently do not use adhesive.

1.1 Study Design

This phase IV study will be a single center, controlled, single blind (with respect to the technician weighing the peanut particles that have migrated under the denture), randomized, two-treatment, two-period, cross-over design, in subjects with full upper and lower dentures. Each treatment period will consist of one day of testing with at least two days between adjacent treatment visits.

A sufficient number of subjects will be screened to randomize 52 subjects to ensure 48 evaluable subjects complete the entire study. Healthy edentulous subjects, between 18 and 85 years of age with both upper and lower dentures will be recruited.

Subjects will be repeated in a cross-over manner. There will be 2-7 days between treatment visits to allow for recovery from the mastication procedures. No washout products will be required for this study.

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1.2 Study Objectives

The objectives to the study are as follows:

Objectives	Endpoints
Primary	
To assess the performance of a marketed denture adhesive (COREGA Maximo Sellado/Selamento) compared to no adhesive in a model for food occlusion.	Mass of peanuts under combined maxillary and mandibular dentures.
Secondary	
To compare the ability of a marketed denture adhesive (COREGA Maximo Sellado/Selamento) to prevent food particle ingress under upper and lower dentures versus no adhesive.	Mass of peanuts under maxillary dentures. Mass of peanuts under mandibular dentures.
To evaluate and compare subject-reported denture dislodgement during a food occlusion methodology when marketed denture adhesive (COREGA Maximo Sellado/Selamento) is used compared to no adhesive.	The number of subject reported denture dislodgements during chewing.
To evaluate and compare subject responses to a questionnaire administered after eating peanuts when using a marketed denture adhesive (COREGA Maximo Sellado/Selamento) compared to no adhesive.	Mean scores from subject-completed questionnaire.
Safety	
To assess the tolerability of marketed denture adhesive (COREGA Maximo Sellado/Selamento).	Treatment emergent adverse events.

This study will be considered successful if there is a statistically significant difference between the mass of peanuts under dentures of subjects using denture adhesive versus when using no adhesive.

1.3 Treatments

In this study COREGA Maximo Sellado/Selamento will be compared to no adhesive. The adhesive will be applied by the clinical site dispensing staff and 1.0 gm (±0.1 gm) will be weighed and applied to the maxillary denture and 0.6 gm (±0.1 gm) will be weighed and applied to the mandibular denture.

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The following study products will be supplied by the Clinical Supplies Department,
GlaxoSmithKline Consumer Healthcare (GSK CH):

Table 1-1   **Investigational/Study Product Supplies**

	Test Product	Control
Product Name	COREGA Maximo Sellado/Selamento	No Adhesive
Pack Design	Precision nozzle tube	N/A
Dispensing Details	N/A	N/A
Product Master Formulation Code (MFC)	CCI	N/A
Dose/Application	1.6 gm of adhesive applied as 1.0 gm (±0.1 gm) for maxillary denture and 0.6 gm (±0.1 gm) for mandibular denture	N/A
Route of Administration	Applied to upper and lower denture which is then placed in mouth	N/A
Usage Instructions	Protocol section 15.4	N/A
Return Requirements	All used/unused samples to be returned to the sponsor	N/A

1.4   Sample Size Calculation

The primary endpoint is the combined mass (mg) of peanuts from both dentures. Based upon a
Modified Intent to Treat (MITT) analysis of a previous study data 208397 using a logarithmic
transformation and an estimate of the within subject variability as the square-root of the (208397
study) Mean Square Error (MSE) (0.5075), 48 subjects in a 2-period crossover design analyzed
with a logarithmic transformation (base 10), will have 81% power to detect a multiplicative
difference of 2 (0.3010 on log scale), that is 2-fold more peanuts (indicating twice as many
peanuts by mass) with no adhesive compared to the active adhesive subjects using a two-sided
significance test at the 5% level. For a multiplicative difference of 2.25 (0.3522 on log scale)
the power will be approximately 91% with 48 evaluable subjects. 52 subjects should be
randomized to ensure 48 subjects are evaluable.

These were calculated using the Power Analysis and Sample Size (PASS) software for a
two-period crossover trial and using the Sw option for the variability estimate as 0.5075. An
extensive simulation study supported the above calculations conducted in PASS.

A non-parametric alternative (Wilcoxon Signed Rank Test) if the logarithmic transformation is
not indicated will have similar power.

2   Planned Analyses

2.1   Interim Analysis

No interim analysis is planned for this study.

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2.2   Final Analyses

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

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

3   Considerations for data analyses and Data Handling Conventions

3.1   Baseline Definition

A baseline definition is not required for this study as no baseline measurements are performed or required for the summaries and analysis.

3.2   Subgroups/Stratifications

No subgroup or stratification factors are included in this study.

3.3   Centers Pools

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

3.4   Timepoints and Visit Windows

The timepoints and visits for this study are defined in the Section 1.1 "Schedule of Activities" of the protocol. Any deviation from the study schedule will be reviewed on case-by-case basis to determine whether the data should be excluded from the Per-Protocol (PP) population. A time window non-compliance listing will be produced for the Blinded Data Review Meeting (BDRM).

4   Data Analysis

Data analysis will be performed by Syneos Health. The statistical analysis software used will be SAS (Studio) 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.

In this study the date and time of start of product application will be the date and time when dentures will be inserted.

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

4.1 Populations for Analysis

4.1.1 Subject Disposition

Screen failures are defined as subjects who consent to participate in the clinical study but are not subsequently randomized. Enrolled subjects are subjects who have signed informed consent and are eligible to proceed beyond the screening visit. The number of subjects screened, enrolled, and randomized will be presented by product sequence and period in Table 14.1.1.

The number and percentage of subjects starting and completing each period and the subjects discontinuing broken down by reason for discontinuation in each period will be presented. The percentage will be computed using the number of subjects starting each period as a denominator.

Subject disposition including the subject status (completer, Yes/No), demographic information (age, gender, and race), screening date, date and time of denture insertion, duration (in days) in the study defined as [(date of completion or withdrawal – date of denture insertion in period 1) + 1] and the specific reason for discontinuation, will be listed (Listing 16.2.1.1) by product sequence.

Subject disposition information for non-randomized subjects will include subject number, demographic information (age, gender and race), screening date, reason for screen failure and details if any regarding the reason for screen failure (Listing 16.2.1.2).

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 (defined below) will be excluded from the PP population.

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

- Consent procedure
- Inclusion/Exclusion criteria
- Study procedure
- Study product compliance

The details of the important protocol deviations and how these will be assessed 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 deviations, important protocol deviations not leading to exclusion from PP population with reasons for

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deviations and subjects with important protocol deviations leading to exclusion from PP
population with reasons for deviations will be presented by product group and overall (Table
14.1.2) and listed in Listing 16.2.2.1.

All protocol deviations collected on the protocol deviation case report form (CRF) 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

The analysis populations defined in study are as follows:

Analysis Population	Definition / Criteria	Analyses Evaluated
Randomized	Any subject who receives a randomization number.	
Safety	All randomized subjects. Receive at least one dose of the study product.	Demographic and Baseline Characteristics Safety Analysis
MITT	All randomized subjects. Receive at least one dose of the study product. Have at least one on therapy assessment of efficacy.	Demographic and Baseline Characteristics Efficacy Analysis
PP	All subject in MITT population. All subject who comply with all study procedures and restrictions that may affect the interpretation of the primary response. Deviations will be determined and applied prior to unblinding and consist of variations in criteria likely to affect the interpretation of the efficacy parameters.	Efficacy Analysis (Primary)

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

Subjects excluded from any of the analysis populations will be listed in Listing 16.2.3.1.

The primary population for assessment of efficacy will be the MITT population. A PP analysis
will be performed on primary endpoint only if 10% or more MITT subjects are excluded from
the PP population. The numbers of subjects included in each of the analysis populations will be
presented in Table 14.1.1, and the number excluded from PP population broken down by the
reason for exclusion will be presented in Table 14.1.2.

4.2   Subject Demographics and Other Baseline Characteristics

Demographic and baseline characteristics summaries will be produced for the safety, MITT,
and PP (if applicable) population.

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4.2.1 Demographic Characteristics

Descriptive statistics (number of subjects [n], mean, standard deviation [SD], median, minimum, and maximum for continuous variables, frequency count [n] and percentage [%] of subjects for categorical variables) will be presented for demographic variables by overall. These variables include age, gender, race, and ethnicity; will be presented for the safety population (Table 14.1.3.1), MITT population (Table 14.1.3.2), and if applicable, on PP population (Table 14.1.3.3).

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

No formal statistical analysis will be performed for this data.

4.2.2 Other Baseline Characteristics

The baseline characteristics will be summarized for all subjects in safety (Table 14.1.4.1), MITT (Table 14.1.4.2), and if applicable on PP (Table 14.1.4.3) population.

Descriptive statistics (n, Mean, SD, Median, Minimum, and Maximum) of duration (years) of denture use and current denture age (years) for each of mandibular and maxillary dentures will be presented by overall.

Frequency count (n) and percentage (%) for secure denture adhesive use, denture bearing tissue score, food migration adequacy for each of the mandibular and maxillary dentures will be presented by overall.

Frequency count (n) and percentage (%) for evaluation of well fit dentures categories (Poor, Fair, Good and Very good) for combined dentures will be provided by overall. Also the descriptive statistics for total score of retention and stability index for combined dentures will be provided by overall.

Complete denture history (Listing 16.2.4.2), denture bearing tissue evaluation (Listing 16.2.4.3), evaluation of well fit dentures (Listing 16.2.4.4), and food migration adequacy (Listing 16.2.4.5) will be listed for all randomized subjects.

No formal statistical analysis will be performed for this data.

4.2.3 General Medical History

Medical history data will be listed (Listing 16.2.4.6) with start date and end date or ongoing at the start of study product on all randomized subjects.

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

Randomization details will be listed, including the randomization number, planned randomized study product sequence, the actual study product sequence subject received and the randomization date (Listing 16.1.7.1).

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4.3.1 Study Product Compliance and Exposure

In this study, COREGA Maximo Sellado/Selamento will be applied directly from the primary product packaging, with 1.0 gm (±0.1 gm) being weighed and applied to the maxillary denture and 0.6 gm (±0.1 gm) being weighed and applied to the mandibular denture.

The weight (gm) of test product applied to the dentures will be summarized descriptively (n, number of missing observations, mean, SD, median, minimum, and maximum) for maxillary, mandibular and combined dentures on all subjects in safety (Table 14.2.1.1) and MITT (Table 14.2.1.2) population. In the combined dentures the sum of weight of adhesive applied to maxillary and mandibular dentures will be obtained.

The study product compliance data will be listed in Listing 16.2.5.1 on all randomized subjects.

4.3.2 Prior and Concomitant Medication

Prior or concomitant medications taken by or administered to the subject will be recorded in the case report form. The prior and concomitant medications will be coded using an internal validated medication dictionary, GSKDrug.

Prior medication will be listed by subject, with drug name, GSK drug synonym, dose, dose form, frequency, route, start date, study day relative to date of dentures were insertion in period 1 and end date (Listing 16.2.5.2). Prior medications are defined as those which stopped before the first study product application. If the stop date is unknown or incomplete and the medication cannot be considered as stopped prior to the first study product application then the medication will be considered as a concomitant medication.

Concomitant medications and significant non-drug will be listed similarly (Listing 16.2.5.3) with either ongoing or end date displayed. Concomitant medications are defined as medications that are ongoing or started on or after the first application of the study products.

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.

The concomitant medication will be assigned to the product received at the time of medication. Ongoing medications at the first period will be assigned to the first product application. Medications starting between periods will be assigned to the product received in the previous period. Medications with a date after last product or the end of the study will be assigned to the product taken in the last period.

4.4 Analysis of Efficacy

The MITT population will be considered as primary population for primary and secondary analysis.

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4.4.1 Primary Endpoint

4.4.1.1 Primary Endpoint Definition

The primary endpoint is defined as the combined mass (mg) of peanuts under maxillary and mandibular dentures.

4.4.1.2 Statistical Hypothesis, Model, and Method of Analysis

Food occlusion will be measured by mass of peanut particles (mass of retrieved peanuts in mg). Primary analysis will be performed on combined values (maxillary and mandibular dentures) of food occlusion.

Descriptive statistics (n, number of missing observations, raw means, geometric mean, SD, standard errors [SE], median, minimum, and maximum values) of combined mass (mg) of peanuts recovered from mandibular and maxillary dentures and their associated gauzes will be provided by product group (Table 14.2.2.1.1) for all subjects in MITT population. This table will also include the summary of mass (mg) of peanuts recovered from individual mandibular and maxillary dentures.

The primary analysis will compare mass of peanuts recovered from the combined dentures between the test product and control.

The null hypothesis for the primary endpoint is that the mass of peanuts obtained from combined dentures is equal between the two groups.

$H_0: \mu_1 = \mu_2$

The alternative hypothesis for the primary endpoint is that the mass of peanuts obtained from combined dentures is not equal between the two groups.

$H_0: \mu_1 \neq \mu_2$

A mixed model analysis of variance (ANOVA) will be used with Log_{10} peanut mass as response and study product and period as fixed explanatory effects and subject as a random effect. The geometric mean, geometric coefficient of variation (CV) and 95% confidence interval (CI) will be presented by study product. The geometric mean ratio, 95% CI and p-value of comparison with no adhesive product group will be presented (Table 14.2.2.1.2). All statistical tests of hypothesis will be two-sided and will employ a level of significance of $\alpha = 0.05$.

In case of many zero counts for mass of peanut particles are obtained, appropriate alternative methods will be explored.

This study will be considered successful if there is a statistically significant difference between the mass of peanuts under dentures of subjects using denture adhesive versus when using no adhesive.

The assumptions underlying the mixed model will be examined using appropriate statistical methods and in case of issue with model assumptions (residual distributions etc.), alternative

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transformations may be sought or non-parametric equivalents (Wilcoxon Signed Rank Test) used.

The bar chart (Figure 14.2.2.1) to display geometric mean and 95% CI of mass (mg) of peanuts recovered in each treatment group from combined dentures will be presented. The geometric mean and CI plotted will be obtained from ANOVA model defined above.

The listing of food occlusion test (Listing 16.2.6.1) by subject, with date and time assessment, weight of peanut particles from maxillary, mandibular and combined dentures will be presented for all subjects randomized.

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 primary efficacy variable will be presented for all subjects in the PP population (Table 14.2.2.2.1) and the same ANOVA model defined for primary analysis will be applied on PP population (Table 14.2.2.2.2).

4.4.2   Secondary Variables

The secondary variables defined in this study are in following section.

4.4.2.1   Secondary Variable 1

The secondary variable 1 is defined as follows:
- Mass (mg) of peanuts under maxillary dentures.
- Mass (mg) of peanuts under mandibular dentures.

4.4.2.2   Secondary Variable 2

The second secondary variable of interest is the number of subject reported denture dislodgements during chewing.

4.4.2.3   Secondary Variable 3

The third secondary variable of interest is mean scores from subject-completed questionnaire.

4.4.3   Handling of Missing Values/Censoring/Discontinuations

Missing observations will not be replaced or imputed. Dropouts will be included in the analysis up to the last assessments at the point of discontinuation.

4.5   Analysis of Secondary Objectives

All secondary analyses will be conducted only on MITT population.

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No alpha adjustments will be made for multiple secondary endpoints due to the exploratory nature of the inferences. All statistical tests of hypothesis will be similar to that mentioned for primary analysis and will be two-sided with 0.05 level of significance.

4.5.1   Efficacy (Secondary)

The analysis of secondary objectives is as follows:

Mass of peanuts under maxillary dentures

Descriptive statistics (n, number of missing observations, raw means, geometric mean, SD, SE, minimum, and maximum values) for the mass (mg) of peanuts recovered from maxillary dentures (Table 14.2.3.1.1) will be provided by product group.

The analysis of mass (mg) of peanuts under maxillary dentures (Table 14.2.3.1.2) will be similar to that mentioned for primary analysis in Section 4.4.1.2.

The bar chart (Figure 14.2.2.2) to display geometric mean and 95% CI of mass (mg) of peanuts recovered in each treatment group from maxillary dentures will be presented. The geometric mean and CI plotted will be obtained from ANOVA model defined for primary analysis in Section 4.4.1.2.

The listing of mass (mg) of peanuts under maxillary dentures will be listed in Listing 16.2.6.1.

Mass of peanuts under mandibular dentures

Descriptive statistics (n, number of missing observations, raw means, geometric mean, SD, SE, minimum, and maximum values) for the mass (mg) of peanuts recovered from mandibular dentures (Table 14.2.4.1.1) will be provided by product group.

The analysis of mass (mg) of peanuts under mandibular dentures (Table 14.2.4.1.2) will be similar to that mentioned for primary analysis in Section 4.4.1.2.

The bar chart (Figure 14.2.2.3) to display geometric mean and 95% CI of mass (mg) of peanuts recovered in each treatment group from mandibular dentures will be presented. The geometric mean and CI plotted will be obtained from ANOVA model defined for primary analysis in Section 4.4.1.2.

The listing of mass (mg) of peanuts under mandibular dentures will be listed in Listing 16.2.6.1.

Number of subject reported denture dislodgements during chewing

The number of denture dislodgements reported by subjects during chewing will be summarized descriptively (n, number of missing observations, raw means, SD, SE, median, minimum, and maximum values) by product group (Table 14.2.5.1.1). Also count and percentage of the individual dislodgements will be provided.

Analysis (Table 14.2.5.1.2) will be performed using a mixed model ANOVA with number of denture dislodgements as response; and treatment and period as fixed explanatory effects and subject as a random effect. The adjusted mean, SE, and 95% CI will be presented by study

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product. The adjusted mean, SE, 95% CI, and p-value of difference between the test product and control will be presented.

The assumptions underlying the mixed model will be examined using appropriate statistical methods and in case of issue with model assumptions (residual distributions etc), alternative transformations may be sought or non-parametric equivalents (Wilcoxon Signed Rank Test) used.

The bar chart (Figure 14.2.2.4) to display adjusted mean and 95% CI of number of denture dislodgements in each treatment group will be presented. The adjusted mean and CI plotted will be obtained from ANOVA model defined above.

The by subject data listing (Listing 16.2.6.2) of number of dislodgements will be produced for all randomized subjects.

Subject-completed questionnaire

For the subjects' response to questionnaires (0-10), descriptive statistics (n, number of missing observations and percentages), mean score and SE of the response will be provided for each question by product group (Table 14.2.6.1.1).

The analysis of subjects' response to questions: amount of peanut pieces under denture (Table 14.2.6.1.2.1) and bothered by peanut pieces under denture (Table 14.2.6.1.2.2) will be performed using the same methods described for the number of dentures dislodgments (Section 4.5.1).

The bar chart to display adjusted mean and 95% CI of subjects' response to questions: amount of peanut pieces under denture (Figure 14.2.2.5) and bothered by peanut pieces under denture (Figure 14.2.2.6) in each treatment group will be presented. The adjusted mean and CI plotted will be obtained from similar ANOVA model defined for the number of dentures dislodgments (Section 4.5.1).

The by subject data listing (Listing 16.2.6.3) of subjects' response to questionnaires will be produced for all randomized subjects.

4.5.2   Pharmacokinetic (Secondary)

Not applicable for this study.

4.6   Analysis of Safety

All safety data will be reported for the safety population as per actual product received. The safety profile of the study treatments will be assessed with respect to adverse events (AEs), oral soft tissue (OST), and incidents.

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4.6.1   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).The AE classified as Oral and Non-Oral will be captured on AE page of CRF.

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

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

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

- Table of treatment-emergent AEs by SOC and PT (Table 14.3.1.1.1). Summary of the number and percentage of subjects with at least one AE, total number of AEs, number and percentage of AEs within each SOC and PT will be displayed.

- Table of treatment-emergent AEs by Oral/Non-Oral and PT (Table 14.3.1.1.2).

- Table of treatment-emergent treatment-related AEs by SOC and PT (Table 14.3.1.2.1).

- Table of treatment-emergent treatment-related AEs by Oral/Non-Oral and PT (Table 14.3.1.2.2).

- Listing of all AEs (Listing 16.2.7.1 for all randomized subjects; Listing 16.2.7.2 for non-randomized subjects).

- Listing of deaths (Listing 14.3.2.1).

- Listing of non-fatal serious AEs (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.

4.6.2   Other Safety Variables

OST examinations will be performed before product application and after the denture removal and peanuts recovery.

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OST will be summarized (number of subjects and percentages) for each parameter by shift table (Table 14.3.1) comparing normal/abnormal results of before product application to after denture removal and peanut recovery. The listing (Listing 16.2.9.1) of OST will provide for all randomized subject and list all the finding obtained at screening visit, before product application and after denture removal and peanut recovery.

All incidents captured in the study will be listed (Listing 16.2.9.2).

4.7 Analysis of Other Variables

The photographs will be presented in the clinical study report and may be included with any publications / presentations arising from this study in order to help explain the study findings.

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5 Changes to the Protocol Defined Statistical Analysis Plan

The changes from the originally planned statistical analysis specified in the protocol are outlined in Table 5-1.

Table 5-1   Changes to the Protocol Defined Analysis Plan

Protocol	Reporting and Analysis Plan	
Statistical Analysis Section	**Statistical Analysis Plan**	**Rationale for Changes**
Section 12.2.2 Definition of Analysis Population • The Per-Protocol (PP) population includes all subjects who fully comply with all study procedures and restrictions. Deviations will be determined and applied prior to unblinding and consist of variations in criteria likely to affect the interpretation of the efficacy parameters.	Section 4.1.3 Analysis Population • PP population includes all subjects in MITT population who comply with all study procedures and restrictions that may affect the interpretation of the primary response. Deviations will be determined and applied prior to unblinding and consist of variations in criteria likely to affect the interpretation of the efficacy parameters.	To add clarification of the definition.

Sodium-calcium mixed partial salt of poly (methylvinylether/maleic acid) and carboxymethylcellulose
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Statistical Reporting and Analysis Plan Text, v1.0 28 Jan 2019

Attachment 1: List of Data Displays

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List of TFLs v1.0_201