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Sodium-calcium mixed partial salt of poly(methylvinylether/maleic acid) and
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CLINICAL PROTOCOL

A Randomised, Open-Label, Clinical Study to Evaluate a Methodology to Assess Food Occlusion Efficacy of a Denture Adhesive in Healthy, Edentulous Subjects.


Compound Name:	Sodium-calcium mixed partial salt of poly(methylvinylether/maleic acid) and carboxymethylcellulose
United States (US) Investigational New Drug (IND) Number:	N/A
European Clinical Trials Database (EudraCT) Number:	N/A
Other Regulatory Agency Identified Number:	N/A
Protocol Number:	208397
Phase:	II

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Sponsor information

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Document History


Document	Version Date	Summary of Changes
Original protocol	20 Oct 2017	Not applicable (N/A)

Amendments incorporate all revisions to date, including amendments made at the request of country health authorities, institutional review boards/ethics committees (IRBs/ECs), etc.

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PRINCIPAL INVESTIGATOR PROTOCOL AGREEMENT PAGE

- I confirm agreement to conduct the study in compliance with the protocol and any amendments and according to the current ICH GCP guidelines.
- I acknowledge that I am responsible for overall study conduct. I agree to personally conduct or supervise the described study.
- I agree to ensure that all associates, colleagues and employees assisting in the conduct of the study are informed about their obligations. Mechanisms are in place to ensure site staff receives all appropriate information throughout the study.
- I agree to conduct this study in full conformance with the laws and regulations of the country in which the research is conducted and the Declaration of Helsinki.

Investigator Name:	Jeffrey L. Milleman
Investigator Qualifications:	DDS, MPA
Investigator Signature:	PPD
Date of Signature/ Agreement:	DD/MMM/YYYY

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SCHEDULE OF ACTIVITIES

The schedule of activities table provides an overview of the protocol visits and procedures.

The investigator may schedule visits (unplanned visits) in addition to those listed on the schedule of activities, in order to conduct evaluations or assessments required to protect the well-being of the subject.

Table 1-1 Schedule of Activities

Procedure/Assessment	Screening	Study Period					
	Visit 1		Visit 2 Treatment Period 1		Visit 3 Treatment Period 2		Visit 4 Treatment Period 3
Informed consent	X	Between 2-30 days		Between 2-30 days		Between 2-30 days	
Review Inclusion/Exclusion criteria	X		X		X		X
Demographics	X						
Medical history	X						
Current / Concomitant treatments	X		X		X		X
Dental history	X						
OST examination edentulous	X		X ^b		X ^b		X ^b
Clean dentures ^c	X		X		X		X
Criteria for well made and fitting dentures (retention, stability, clinical acceptability and denture finish)	X						
Food migration adequacy	X						
Subject eligibility	X						
Urine pregnancy test ^e			X		X ^d		X ^d
Randomisation			X				
Subject continuance			X		X		X
Treatment application and denture insertion ^a			X		X		X
Efficacy assessment - Food occlusion testing			X		X		X
Efficacy assessment - Number of denture dislodgements			X		X		X
Photograph of dentures (subset of subjects)			X		X		X
Subject-completed questionnaire			X		X		X
Adverse events			X		X		X
Incidents	X		X		X		X
Study conclusion							X

Abbreviations: OST = Oral Soft Tissue.

Any serious adverse event assessed as related to study participation that occurs subsequent to the signing of informed consent and any adverse event that occurs subsequent to the first dose will be recorded.

a There will be a 60±5 minute wait after dentures are inserted and the commencement of the food occlusion testing.

b At visits 2-4 the OST examination will be performed before product application and also after the denture removal and peanut recovery.

c Dentures will be cleaned both prior to and after the food migratory adequacy (V1) or food occlusion testing assessment (V2-4).


d Pregnancy testing at Visits 3 and 4 are only required should more than 30 days have elapsed between the treatment visit and the previous pregnancy test.

e For females of childbearing potential per Section 7.3.2.

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1 INTRODUCTION

Denture adhesives serve to increase the retentive hold of dentures to the oral mucosa and may also reduce the ingress of food particles under the denture. Such particles can lead to irritation of the mucosa and is often a major concern to the denture wearer. Current understanding suggests that restriction of food particle ingress is achieved through a tighter denture fit provided by the denture adhesive through its ability to both adhere the denture to the mucosa and to occlude gaps between the denture and the mucosa which might otherwise be susceptible to food particle ingress ([Özcan, 2005](#)). The increased adherence to the mucosa leads to reduced movement of the denture whilst chewing, leading to a reduction in particle migration under the denture ([Tarbet, 1980](#)). Additionally, the hydration of denture adhesives through contact with saliva leads to expansion of the adhesive, occluding gaps between the denture and the underlying mucosa ([Özcan, 2005](#)). The adhesive can therefore be thought of as forming a seal along the denture borders which prevents ingress of small food particles.

Published methodologies for evaluating the performance of a denture adhesive at reducing the ingress of food particles under the denture are rather limited in numbers. Tarbet *et al* ([Tarbet, 1980](#)) had subjects subjectively rate (on a ten-point scale) whether they experienced less food particles under their dentures after eating foods including celery, steak, taffy apples and sandwiches when using a denture adhesive compared to no adhesive. This study showed a statistically significant difference ($p < 0.01$) in subjective score in favour of use of adhesive compared to no adhesive use. Ahmad *et al* ([Ahmad, 2009](#); [Ahmad, 2010](#)) described a quantitative methodology based upon having fully edentulous subjects chew a prescribed amount of peanuts while wearing both their maxillary and mandibular dentures. After chewing the peanuts, the subjects brushed their dentures whilst still wearing them, rinsed with water then removed their dentures. Study staff then removed the peanut particles from the fit surfaces of the dentures and any adhesive from the dentures and the denture bearing tissues, washed and sieved the peanut particles and dried the particles prior to weighing them. This study was able to show statistically significant lower weight of peanuts collected between subjects using an adhesive compared to no adhesive use. The weight of peanut particles recovered was not reported in full, however a mean weight of 51mg and 35mg was found for maxillary dentures for the adhesive and no-adhesive treatment groups respectively.

GSK have previously sponsored studies at the University of Buffalo using a similar methodology to Ahmad ([L3510566, 2008](#); [Munoz, 2012](#)). The inclusion criterion for Kapur (Olshan modified) was, however, less stringent, allowing subjects with a score ≥ 6 to be enrolled. In this study two cream adhesives and a strip adhesive were compared to the use of no adhesive. For the cream adhesives, a total of 1.6g was used split as 1.0g for maxillary and 0.6g for mandibular dentures. The adhesive was applied as 3 short strips on the maxillary and 2 short strips on the mandibular dentures. For the strips, 3 were used for the maxillary dentures and 2 for the mandibular dentures. Peanut consumption occurred 2 hours after denture insertion. This study found there was no difference in the mass of peanut particles migrated under the dentures between any of the test groups, and that the mass of particles recovered was small, ≤ 20 mg for combined mass from both maxillary and mandibular dentures

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for each subject. Further studies by the same principle investigator (PI) did demonstrate the ability of denture adhesives to restrict the ingress of food under a dentures in studies of full (CCI [REDACTED]; Munoz-Viveros, 2010) and partial (Munoz-Viveros, 2010; CCI [REDACTED] denture wearers. These studies used modified chewing and laboratory procedures and more stringent inclusion criteria. These studies all demonstrated statistically significant reductions in food particle entrapment when using an adhesive compared to the use of no adhesive.

Following the loss of the clinical facility at University of Buffalo, GSK sponsored a study (205915, 2016) run at Salus Research using a similar methodology, but this study was unable to demonstrate a difference in peanut migration between use of an adhesive and no adhesive. A key difference between the Salus study and the previous Buffalo studies was the method of application of the adhesive to the denture.

The aim of this study is to establish a reliable methodology that is able to characterise the performance of the adhesive in terms of reducing food ingress in a food occlusion methodology where subjects are asked to eat peanuts in a controlled manner and the mass of peanut particles under the denture, post peanut consumption, is measured and compared.

This study will be conducted at Salus Research in the USA.

1.1 Mechanism of Action/Indication

Sodium-calcium mixed partial salt of poly(methylvinylether/maleic acid) and carboxymethylcellulose is currently included in a denture adhesive marketed by GSK. Denture adhesives function by forming an adhesive layer between the denture and gum surface that can act as a physical shield which can help reduce the ingress of food particles.

This study will be conducted in patients with complete maxillary and mandibular dentures.

1.2 Background and Rationale

The aim of this method development study is to assess if the changes made to the operational procedures from study 205915 result in an improved successful differentiation between the use of a denture adhesive and no denture adhesive in a model of food occlusion.

1.2.1 Study Design Rationale


Based on previous findings, the peanut occlusion methodology has demonstrated the ability to detect differences in the mass of peanut particulate measured, and this protocol will continue to use the adhesive dissolution and peanut retrieval steps utilised in GSK studies (CCI [REDACTED])

Whilst the objective measure of peanut mass is the primary endpoint of interest in this study, subject derived opinion of efficacy will also be measured by means of a subject-completed questionnaire. The number of denture dislodgements reported by the subjects during the chewing of the peanuts will also be collected and analysed and this, and the questionnaire data, will be used to support the findings of the peanut mass measure.

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Dentures are unique to each individual. Therefore, the most efficient approach to evaluating their performance with different adhesives or 'no adhesive' is a within subject comparison (i.e. a crossover design). Denture adhesive is used to secure dentures in the mouth. It forms a barrier that prevents food from entering the area between dentures and the edentulous ridge. This study will assess the objective measure of food occlusion while chewing peanuts as measured by mass of peanuts retrieved, as well as subjective measures of efficacy as measured by questionnaire data.

Peanuts were chosen as the model food in this methodology because they are a brittle food that, when masticated, break into small particles that can be recovered. Peanuts have therefore been retained as a model food for this study and to allow comparison with previous data.

In order for subjects to be eligible they must report that they get food trapped under their dentures and this must be evident following the standardised peanut migration adequacy testing at screening (Visit 1). This is to ensure that measurable amounts of peanut particles migrate under the denture when no denture adhesive is being used. Whilst peanut allergy is specific, peanuts supplied for this study may themselves be contaminated with other nuts owing to the manufacturing process. Therefore, subjects with any nut allergy are excluded from this study. Subjects with temporomandibular joint disorders are excluded should the investigator believes that this could affect the subject's participation, principally regarding the ability for the subject to adequately chew the peanuts. Subjects who use or have ever used bisphosphonate medications are specifically excluded from this study owing to the enhanced risk of bisphosphonate-related osteonecrosis of the jaw (BRONJ) that is associated with reduced tissue tolerance to function with removable prostheses ([Saldanha, 2012](#)). Subjects in this study must be habitual wearers of full dentures to ensure that they are familiar with chewing with their dentures in place. Subjects who are xerostomic are excluded since the proper function of denture adhesives requires adequate hydration from saliva.

During this study, photographs of dentures with peanut particles attached will be taken. The purpose of this is to gather representative photographs of the dentures to aid in the dissemination and interpretation of the results, e.g. in manuscript preparation. No personally identifiable information will be included in these photographs. Demography information will be recorded as part of this study, including age, race and gender. In accordance with the United States Food and Drug Administration (US FDA) guidelines ([FDA, 2005](#)) the ethnicity of subjects will also be captured.

An oral soft tissue (OST) examination will be conducted at each treatment visit before treatment is applied to ensure the subject's oral health is sufficient to allow the subject to complete the assessments at that visit. A further OST exam will be performed at each treatment visit after the completion of assessments to assess for possible AEs.

Whilst blinding is an important consideration for any clinical study, the objectives of this study are not to investigate product efficacy, but to develop a methodology. To fulfil the objectives of this study it is not possible to adequately maintain blinding and therefore this study will be conducted open label.

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The Kapur-Olshan index is a composite score based upon stability and retention ratings for the maxillary and mandibular dentures ([Kapur, 1967](#); [Olshan, 1992](#)). In this study, subject recruitment will be targeted to achieve approximately equal numbers of subjects in the low and high Kapur-Olshan groups. The low Kapur-Olshan group is defined as a composite Kapur-Olshan score of 6-14 (clinically fair and good dentures) and the high Kapur-Olshan score as 15-18 (clinically very good dentures), values derived from consideration of previous study data ([205915, 2016](#)). The purpose of this analysis is to explore the optimum inclusion criteria for future studies. Subjects presenting with a very low Kapur-Olshan score at Screening (<6), defined as "Clinically Poor" ([Olshan, 1992](#)), will be excluded from this study.

Denture adhesive achieves its function by physical means and once completely removed from the denture does not have any residual effects. Therefore, the 2-30 day period between each test day is considered adequate rest for the oral soft tissues from the stresses of mastication encountered in this study.

Marketed denture adhesives are commonly extruded by the consumer onto the denture either through a flat ribbon nozzle with instructions for use to "dab" the product onto the denture (the conventional application pattern) or through a finer nozzle that enables the adhesive product to be more precisely applied so allowing a continuous bead of product around the borders of the dentures (continuous strips application pattern). In this method development study both application methods will be evaluated, with the adhesive applied via a syringe, to assess if the methodology is compatible with either or both application methods. The use of the syringe allows for greater control of dose and application pattern and is consistent with previous studies.


1.2.2 Treatments

Three treatment arms will be used in this cross-over study:-

- Super Poligrip Free (USA marketplace) applied via a conventional pattern.
- Super Poligrip Free (USA marketplace) applied via a continuous strips pattern.
- No adhesive.

A single, common adhesive will be used (Super Poligrip Free) with a common dose (1.6g) for both application methods. The adhesive will be extruded from a pre-dosed syringe following the application instructions. Super Poligrip Free has been selected as the adhesive in this study as it is a currently marketed product and is considered a representative denture adhesive. 1.6g of adhesive per treatment will be applied to each subject's dentures, an amount consistent with that used in previous studies and will therefore facilitate comparison of data from this study with previous work. This dose will be split as 1.00 ± 0.05 g for the maxillary and 0.60 ± 0.05 g for the mandibular dentures in accordance with consumer's normal distribution of adhesive.

A no adhesive negative control treatment has been chosen to provide a continual reference point to allow interpretation of the results and to facilitate comparison of the results from this

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study with previous work, and is representative of a significant number of denture wearers who currently do not use an adhesive.

Complete information for this compound may be found in the single reference safety document (SRSD), which for this study is the Safety Statement.

2 STUDY OBJECTIVES AND ENDPOINTS

Table 2-1 Study Objectives and Endpoints

Objectives	Endpoints
Primary	
To evaluate the mass of peanut particles that migrate under the dentures during a food occlusion methodology when denture adhesive is applied per conventional pattern.	Mass of peanuts under combined maxillary and mandibular dentures.
Exploratory	
To evaluate the mass of peanut particles that migrate under the dentures during a food occlusion methodology when denture adhesive is applied per continuous strips pattern and when no adhesive is used.	Mass of peanuts under combined maxillary and mandibular dentures.
To evaluate the mass of peanut particles that migrate under the maxillary and mandibular dentures during a food occlusion methodology when denture adhesive is applied per conventional pattern, continuous strips pattern and when no adhesive is used.	Mass of peanuts under maxillary dentures. Mass of peanuts under mandibular dentures.
To evaluate subject responses to 2 questions during a food occlusion methodology when denture adhesive is applied per conventional pattern, continuous strips pattern and when no adhesive is used.	Subject completed questionnaire.
To explore the performance of a marketed denture adhesive when applied per conventional pattern to no adhesive use for subjects in the low and high Kapur-Olshan subgroups.	Mass of peanuts under combined maxillary and mandibular dentures in each subgroup (low and high Kapur-Olshan scores).
To explore the relationship between the number of subject-reported denture dislodgements when denture adhesive is applied per conventional pattern, continuous strips pattern and when no adhesive is used.	The number of subject reported denture dislodgements during chewing.
Safety	
To assess the tolerability of marketed denture adhesive (Super Poligrip Free).	Treatment emergent adverse events.

This study is a method development study and therefore there is no formal success criterion.

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3 STUDY DESIGN AND SUBJECT POPULATION

This will be a single centre, controlled, open label, randomised, three-treatment, three-period, cross-over design in subjects with full upper and full lower dentures. Each treatment period will consist of one day of testing with at least two days between adjacent treatment visits.

Approximately 48 (maximum 50) healthy subjects with both maxillary and mandibular full dentures will be enrolled in this study. In this study, subject recruitment will be targeted to achieve approximately equal numbers of subjects in the low and high Kapur-Olshan groups. The low Kapur-Olshan group is defined as a composite Kapur-Olshan score of 6-14 (clinically fair and good dentures) and the high Kapur-Olshan score as 15-18 (clinically very good dentures).

At the screening visit, following an OST examination, each subject's dentures (upper and lower) will be cleaned then assessed for retention and stability using the Kapur Index (Olshan Modification) ([Kapur, 1967](#); [Olshan, 1992](#)) and whether they are well made. Only those subjects with dentures (both upper and lower) that satisfy both of these criteria will undergo the food migration adequacy assessment to provide evidence of adequate peanut particle migration under the dentures after chewing a portion of peanuts. A visual observation and rating of location and extent of peanut particle migration adequacy must indicate > 0 on a 0 – 3 scale. Subjects meeting all the inclusion criteria with no exclusions will then be randomised at Visit 2. Subject recruitment will be controlled to ensure 50±10% of the subjects will be in each of the low and high Kapur-Olshan groups [the low Kapur-Olshan group is defined as a composite Kapur-Olshan score of 6-14 (clinically fair and good dentures) and the high Kapur-Olshan score as 15-18 (clinically very good dentures)]. There will be between 2-30 days between the screening visit and the for test day.


On each test day (Visits 2-4) subjects will undergo an OST examination and have their dentures cleaned. Treatment (or no treatment as per the randomisation schedule) will then be applied as per the application instructions and the dentures worn by the subject. Then, 60±5 minutes after inserting their dentures each subject will be given a standardised portion of peanuts to consume, following a prescribed chewing and swallowing method. Whilst chewing the peanuts subjects will record the number of denture dislodgements that occur during the chewing procedure. After this, subjects will rinse their mouth with water. The examiner will then remove the lower denture and any peanut particles or adhesive remaining on the mandibular ridge will be removed using gauze. The examiner will then remove the upper denture and any peanut particles or adhesive remaining on the palate will be removed using new gauze. The subject will then complete a questionnaire on efficacy and a further OST examination will be performed.

For a subset of subjects the fit surface of their dentures will be photographed before peanuts are collected from the fit surface. These subjects will be selected at the discretion of the Investigator, but allow for a variety of denture sizes and fit to be represented. It is expected that approximately 5 sets of dentures be photographed per treatment group, and where possible that consistency of subjects between treatments is maintained (i.e. a subject will be identified at visit 2 as being suitable for denture imaging and will have their dentures

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photographed at visits 2, 3 and 4 however, should subject dropouts or other reasons necessitate, subjects can be substituted).

Peanut particles will then be collected from the fit surfaces of the dentures and the gauzes and weighed to evaluate the mass of food particles that had migrated under the denture (keeping the particles associated with the upper and lower dentures separate).

These procedures will be repeated in a crossover manner. There will be between 2-30 days between treatment visits to allow for recovery from the mastication procedures.

Safety will be assessed by examination of the oral soft tissues at the Screening Visit and before and after each treatment assessment has been completed at each of the treatment visits. Abnormalities reported after the subject's first use of treatment will be considered as adverse events (AEs). Incidents will be recorded from the first use of a medical device.

4 SUBJECT SELECTION

This study can fulfil its objectives only if appropriate subjects are enrolled. The following eligibility criteria are designed to select subjects for whom participation in the study is considered appropriate. All relevant medical and nonmedical conditions should be taken into consideration when deciding whether a particular subject is suitable for this protocol.

4.1 Inclusion Criteria

Subject eligibility should be assessed and documented by an appropriate member of the investigator's study team before subjects are enrolled in the study.

Subjects must meet all of the following inclusion criteria to be eligible for enrolment into the study:

- 1) Evidence of a personally signed and dated informed consent document indicating that the subject has been informed of all pertinent aspects of the study before any assessment is performed.
- 2) Male or female who, at the time of screening, are between the ages of 18 and 85 years, inclusive.
- 3) Willing and able to comply with scheduled visits, treatment plan, and other study procedures.
- 4) Healthy, defined as in general good physical health, as judged by the investigator.
- 5) Self-reports experience of getting food trapped under their denture.
- 6) Is an habitual wearer of both of their dentures defined as subjects who wear both of their dentures for the majority of their time whilst awake.
- 7) Females of childbearing potential and at risk for pregnancy must agree to use a highly effective method of contraception throughout the study and for 1 day after the last dose of assigned treatment. Female subjects who are not of childbearing potential must meet requirements in [Section 4.4.2](#).
- 8) Have denture prostheses that fulfil all of the following:

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- A qualifying conventional acrylic full denture in both the upper and lower arch.
- Dentures are well fitting (Kapur (Olshan Modification) Retention and Stability Index Sum Score ≥ 6) ([Olshan, 1992](#)) with no individual stability or retention scores < 1 .
- Dentures are well made (according to the well-made assessment).
- Has a peanut particle migration rating > 0 for each denture.

4.2 Exclusion Criteria

Subjects who meet any of the following exclusion criteria will not be eligible for enrolment in the study:

- An investigational site staff member directly involved in the conduct of the study or their family member, site staff members otherwise supervised by the investigator, or an employee of the sponsor directly involved in the conduct of the study.
- Participation in any other clinical study involving investigational drugs, cosmetics or medical devices within 30 days prior to study entry and/or during study participation.
- Acute or chronic medical or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation or investigational product administration or may interfere with the interpretation of study results and, in the judgment of the investigator, would make the subject inappropriate for entry into this study.
- Pregnant female subjects.
- Breastfeeding female subjects.
- Known or suspected intolerance or hypersensitivity to the study materials (or closely related compounds) or any of their stated ingredients.
- Unwilling or unable to comply with the Lifestyle Guidelines described in this protocol.
- History of swallowing difficulties or choking.
- Currently taking or have taken a bisphosphonate drug (i.e., Fosamax[®], Actonel[®], Boniva[®]) for treatment of osteoporosis.
- Any clinically significant or relevant oral abnormality (e.g. temporomandibular joint [TMJ] problems) that, in the opinion of the investigator, could affect the subject's participation in the study.
- Known allergy to peanuts or any other nut.
- Any condition or medication which, in the opinion of the investigator, is currently causing xerostomia.
- Recent history (within the last year) of alcohol or other substance abuse.
- OST examination findings such as stomatitis, open sores, lesions, redness or swelling which in the opinion of the investigator, would interfere with the conduct of the study.

[®] Fosamax is a registered trademark of Merck & Co.

[®] Actonel is a registered trademark of Warner Chilcott Company, LLC.

[®] Boniva is a registered trademark of Genentech.

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15. Use of any medication that, in the opinion of the investigator, would interfere with the conduct of the study.

16. A serious chronic disease requiring intermittent hospital visits.

17. Having been previously enrolled in this study.

18. Any subject who, in the opinion of the investigator, should not participate in the study.

4.3 Randomisation Criteria

Subjects will be randomised into the study provided they have satisfied all subject selection criteria. Subjects should be recruited so that, at screening, approximately 50% (40-60%) of the subject population attains a Kapur-Olshan Score of 6-14 and approximately 50 % (40-60%) attains a Kapur-Olshan Score of 15-18.

4.4 Lifestyle Guidelines

During the entire study (screening – LSLV):

- Subjects will not be permitted to have any dental/denture work performed during the time they are in the study, unless discussed and permitted by the examiner. This is to assure that the denture fit will not be altered during the study.
- Subjects are not permitted to use of bisphosphonates as per exclusion criterion 9.

During the treatment visits (Visits 2-4):

- Subjects will not be allowed to use tobacco or nicotine-containing products following denture insertion until after their dentures are returned at completion of the food occlusion testing.
- Subjects will not be able to use any oral healthcare product other than those supplied by the investigator following denture insertion until after their dentures are returned at completion of the food occlusion testing.

4.4.1 Meals and Dietary Restrictions

Subjects will not be allowed to consume any food (including chewing gum) or drinks following denture insertion until after their dentures are returned at completion of the food occlusion testing (with the exception of small sips of water to alleviate thirst, to aid chewing the peanuts or to assist with medication).


4.4.2 Contraception

All female subjects who are of childbearing potential and are sexually active and at risk for pregnancy must agree to use a highly effective method of contraception consistently and correctly for the duration of the active study period and for 1 day after the last dose of investigational product. The investigator or designee, in consultation with the subject, will confirm verbally that the subject is using one of the methods of contraception from the permitted list of contraception methods (see below) and has been instructed by a medically qualified individual in its consistent and correct use. Subjects need to affirm that they meet

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the criteria for the correct use of at least 1 of the selected methods of contraception. The investigator or his or her designee will discuss with the subject the need to use highly effective contraception consistently and correctly according to the schedule of activities and document such conversation in the subject's chart. In addition, the investigator or his or her designee will instruct the subject to call immediately if the selected contraception method is discontinued or if pregnancy is known or suspected in the subject.

Highly effective methods of contraception are those that, alone or in combination, result in a failure rate of less than 1% per year when used consistently and correctly (i.e., perfect use) and include the following:

1. Established use of oral, inserted, injected, transdermal, or implanted hormonal methods of contraception is allowed provided the subject plans to remain on the same treatment throughout the entire study and has been using that hormonal contraceptive for an adequate period of time to ensure effectiveness as deemed appropriate by the investigator.
2. Correctly placed copper-containing intrauterine device (IUD).
3. Male condom or female condom used WITH a spermicide (i.e., foam, gel, film, cream, or suppository). For countries where spermicide is not available or condom plus spermicide is not accepted as highly effective contraception, this option is not appropriate.
4. Male sterilisation with absence of sperm in the post-vasectomy ejaculate.
5. Bilateral tubal ligation / bilateral salpingectomy or bilateral tubal occlusive procedure (provided that occlusion has been confirmed in accordance with the device's label).
6. Female who meets the criteria for non-childbearing potential as described below.

Female subjects of non-childbearing potential must meet at least one of the following criteria:

- a. Achieved postmenopausal status, defined as follows: cessation of regular menses for at least 12 consecutive months with no alternative pathological or physiological cause; status may be confirmed by having a serum follicle-stimulating hormone (FSH) level confirming the post-menopausal state;
- b. Have undergone a documented hysterectomy and/or bilateral oophorectomy;
- c. Have medically confirmed ovarian failure.

All other female subjects (including females with tubal ligations) will be considered to be of childbearing potential.

4.5 Screen Failures

Screen failures are defined as subjects who consent to participate in the clinical study but are not subsequently randomised. To ensure transparent reporting of screen failure subjects, a minimal set of screen failure information will include demography, screen failure details (e.g., withdrawal of consent), eligibility criteria, and any serious adverse events (SAEs).

Individuals who do not meet the criteria for participation in this study (screen failure) may not be re-screened.

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4.6 Sponsor's Qualified Medical Personnel

The contact information for the sponsor's appropriately qualified medical/dental personnel for the study is documented in the study contact list located in the Study File.

The contact number can be used by investigational staff if they are seeking advice on medical/dental questions or problems; however, it should be used only in the event that the established communication pathways between the investigational site and the study team are not available. It is therefore intended to augment, but not replace, the established communication pathways between the investigational site and the study team for advice on medical/dental questions or problems that may arise during the study. The contact number is not intended for use by the subject directly, and if a subject calls that number, he or she will be directed back to the investigational site.

To facilitate access to appropriately qualified medical/dental personnel on study-related medical/dental questions or problems, subjects are provided with a contact card. The contact card contains, at a minimum, protocol identifiers, subject study numbers, contact information for the investigational site, and contact details in the event that the investigational site staff cannot be reached to provide advice on a medical question or problem identified from the subject's healthcare professional other than the investigator.


5 STUDY TREATMENTS

5.1 Blinding and Allocation to Treatment/Randomisation

Treatments will be provided in an open-label manner. No members of the study team will be blinded to the treatment allocation. The investigator's knowledge of the treatment should not influence the decision to enrol a particular subject or affect the order in which subjects are enrolled.

InVentiv Health will provide a randomisation schedule to the study site. This consists of a series of randomisation numbers. Each randomisation number lists 3 corresponding alphabetic treatment codes, with a unique code assigned for each of the 3 treatment periods (e.g. treatment period 1=B, treatment period 2=A, treatment period 3=C). The schedule will also detail which treatment code corresponds to each of the 3 treatments detailed in [Section 5.3](#). At Visit 2, each subject who fulfils all the inclusion criteria and none of the exclusion criteria will be assigned the lowest available randomisation number (each randomisation number should only be assigned to a single subject). The sequence of treatments for each randomised subject can therefore be read from the randomisation schedule for that subject's randomisation number. The corresponding randomisation treatment code will also be printed on the supplied product application instruction sheets for the treatments except for the "no adhesive" treatment. Specific training on this procedure will be carried out at the Site Initiation Visit.

Subject recruitment will be controlled to ensure 50±10% of the subjects will be in each of the low and high Kapur-Olshan groups [the low Kapur-Olshan group is defined as a composite

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Kapur-Olshan score of 6-14 (clinically fair and good dentures) and the high Kapur-Olshan score as 15-18 (clinically very good dentures)].

5.2 Subject Compliance

Study treatment will be administered under the supervision of investigator site personnel and documented in the CRF.

5.3 Investigational Product Supplies

The following study products will be supplied by the Clinical Supplies Department, GSKCH:

	Test Product (Conventional Application)	Test Product (Continuous Strips Application)	Negative Control
Product Name	Super Poligrip® Free Denture Adhesive Cream (USA Marketplace)	Super Poligrip® Free Denture Adhesive Cream (USA Marketplace)	No Adhesive
Product Formulation Code	CCI	CCI	N/A
Dose	1.6g of adhesive applied as 1.0g for maxillary denture and 0.6g for mandibular denture.	1.6g of adhesive applied as 1.0g for maxillary denture and 0.6g for mandibular denture.	N/A
Route of Administration	Applied to denture which is placed in mouth	Applied to denture which is placed in mouth	N/A
Dosing Instructions	As per the Product Application Instructions	As per the Product Application Instructions	N/A

Other items to be supplied by the Clinical Supplies Department, GSKCH:

- Oral B® Denture brushes - to clean dentures.
- Polident® Dentu Crème Denture cleansing paste (USA marketplace)- to clean dentures.
- Syringes - to apply adhesive to dentures.
- Syringe caps - to protect pre-filled syringes.
- Pregnancy test kits.

* Poligrip is a registered trademark of GlaxoSmithKline Consumer Healthcare.

* Oral B is a registered trademark of Proctor & Gamble.

* Polident Dentu Crème is a registered trademark of GlaxoSmithKline Consumer Healthcare.

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5.3.1 Dosage Form and Packaging

The test product is intended for oral use, and will be administered orally as detailed in the [Product Application Instructions](#). The test product will be supplied by GSK CH in commercially marketed tubes sourced from the USA marketplace. The contents of the product label will be in accordance with all applicable regulatory requirements and will be the responsibility of the Global Clinical Supplies Department, GSK CH.

All sundry items will be supplied in their commercial packaging for use by study staff as required.

Care should be taken with the supplied products and their labels so that they are maintained in good condition. It is important that all labels remain intact and legible for the duration of the study.

5.3.2 Preparation and Dispensing

To ensure consistency of treatment product, prior to the first use of each tube of denture adhesive, the first 1-2 inches of adhesive shall be extruded and disposed. Supplied syringes will be filled by the site personnel so that they contain 1.00 ± 0.05 g or 0.60 ± 0.05 g of test denture adhesive for application to the maxillary and mandibular dentures respectively. Syringes can be pre-filled in advance of the application, but must be stored capped and must not be stored for longer than 4 hours after loading. The mass of adhesive in each syringe, the time of loading and the time the dentures are placed in the mouth will be recorded in a dispensing log and the CRF. Syringes will be labelled with the subject or randomisation number and identifying text for maxillary or mandibular application.

5.4 Administration

Subject's dentures will first be cleaned prior to application of adhesive, or no adhesive. Using the supplied denture brush and cleansing paste, both the upper and lower dentures will be thoroughly cleaned to remove all traces of denture fixative, plaque and particulates/debris. Dentures should then be dried.

Adhesive is applied to dentures by extruding all of the pre-weighed adhesive from syringes onto the dentures per the [Product Application Instructions](#). The dentures will then be returned to the subject who should reposition the dentures in their mouth and bite down to secure hold. For subjects on the "no adhesive" treatment visit, the dentures should be cleaned and dried as above, then refitted by the subject.

5.4.1 Medication Errors

Medication errors may result, in this study, from the administration or consumption of:

- the wrong product,
- by the wrong subject,
- at the wrong time,

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- or at the wrong dosage amount (other examples of concern may be added based on the investigational product administration, such as inadvertent exposure).

Such medication errors occurring to a study participant are to be captured in the CRF. In the event of medication dosing error, the sponsor should be notified immediately.

Medication errors are reportable irrespective of the presence of an associated AE/SAE, including:

- Medication errors involving subject exposure to the investigational product;
- Potential medication errors or uses outside of what is foreseen in the protocol that do or do not involve the participating subject.

Whether or not a medication error is accompanied by an AE, as determined by the investigator, the medication error and, if applicable, any associated adverse event(s) is captured on an adverse event (AE) CRF page.

5.5 Investigational Product Storage

The investigator, or an approved representative will ensure that all investigational products are stored in a secured area with controlled access under required storage conditions and in accordance with applicable regulatory requirements and product label.

Site systems must be capable of measuring and documenting (for example, via a log), at a minimum, daily minimum and maximum temperatures for all site storage locations (as applicable, including frozen, refrigerated, and/or room-temperature products). This should be captured from the time of investigational product receipt throughout the study. Even for continuous monitoring systems, a log or site procedure that ensures active daily evaluation for excursions should be available. The operation of the temperature-monitoring device and storage unit (for example, refrigerator), as applicable, should be regularly inspected to ensure it is maintained in working order.

Any excursions from the product-label storage conditions should be reported upon discovery. The site should actively pursue options for returning the product to the storage conditions as described in the labelling, as soon as possible. Deviations from the storage requirements, including any actions taken, must be documented and reported to the Sponsor.

Once an excursion is identified, the investigational product must be quarantined and not used until the Sponsor provides documentation of permission to use the investigational product. It will not be considered a protocol deviation if the sponsor approves the use of the investigational product after the temperature excursion. Use of the investigational product prior to sponsor approval will be considered a protocol deviation. Specific details regarding information the site should report for each excursion will be provided to the site.


5.6 Investigational Product Accountability

All products supplied are for use only in this clinical study and should not be used for any other purpose.

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Study treatments must be received by a designated person at the study sites, handled and stored safely and properly, and kept in a secured location to which only the staff have access. Upon receipt, all study treatments should be stored according to the instructions specified on the treatment labels. Clinical supplies are to be dispensed only in accordance with the protocol.

The clinical study site must maintain adequate records documenting the receipt, use, loss, or other disposition of the investigational product supplies. All study products will be accounted for using a drug accountability form/record.

The inventory must be available for inspection by the study monitor during the study. Monitoring of treatments accountability will be performed by the field monitor during site visits and at the completion of the study.

5.6.1 Destruction of Investigational Product Supplies

All investigational study treatments shipped for this clinical trial will be returned to the Sponsor at the termination of the study. At the conclusion of the study, the Principal Investigator or an appropriate designee, and a representative of GSK CH will inventory all used and unused investigational study treatment. The study treatment inventory record for returned study treatment will then be completed. All investigational product for this clinical study (empty containers), as well as all unused study product will be returned to the designated vendor using the return shipping instructions provided.

5.7 Concomitant Treatments

Details of any relevant dental, medical or surgical history (within the last year), including allergies or drug sensitivity, will be recorded in the CRF. The use of concomitant medications is permitted in this study with the exception of the use of bisphosphonate drugs (exclusion criterion 9) and medications that in the opinion of the investigator would interfere with the conduct of this study (exclusion criterion 15).

Treatments taken after the first dose of study investigational product will be documented as concomitant treatments.

All concomitant treatments taken during the study must be recorded with indication, unit dose, daily dose, and start and stop dates of administration. All subjects will be questioned about concomitant treatment at each clinic visit.

Subjects will be asked not to have any non-emergency dental/denture work performed during the time they are in the study, unless discussed and permitted by the examiner. This is to assure that the denture fit will not be altered during the study.

5.8 Rescue Medication

No specific rescue therapy is required in this study. Should a subject suffer an adverse reaction to the peanuts consumed in this study then the study staff will administer appropriate first aid including use of adrenaline in the case of anaphylaxis.

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6 STUDY PROCEDURES

6.1 STUDY PERIOD

6.1.1 Screening - Visit 1

The following procedures/assessments will take place in the order listed below (where possible), and recorded in the CRF:

- Obtain written informed consent.
- Collect demography (year of birth, gender, race and ethnicity).
- Obtain medical history, including history of illegal drug, alcohol and tobacco use.
- Obtain [Dental History](#).
- Obtain complete medication history of all prescription or non-prescription drugs, and dietary and herbal supplements taken within 30 days prior to the planned first dose.
- Perform [OST Examination-Edentulous](#).
- Clean the subject's dentures using the supplied denture brush and cleansing paste, both the upper and lower dentures will be thoroughly cleaned to remove all traces of denture fixative, plaque and particulates/debris. Dentures should then be dried.
- Perform the [Well-Made Assessment](#).
- Perform the [Well-Fit Assessment](#).
- Perform the [Food Migration Adequacy Assessment](#).
- Review Inclusion and Exclusion criteria. Pregnancy status will be confirmed verbally by the subject.
- Assess subject eligibility.
- Any serious adverse event assessed as related to study participation that occurs subsequent to the signing of informed consent will be recorded.

To prepare for study participation, subjects will be instructed on the use of the [Lifestyle Guidelines](#) and [Concomitant Treatment\(s\)](#) sections of the protocol.

6.1.2 Visit 2


Subjects will be admitted to the clinical site between 2-30 days after Screening. The following procedures will be completed in the following order (wherever possible) and recorded in the CRF:

- Review Inclusion and Exclusion criteria. Pregnancy status will be confirmed verbally by the subject.
- Collect urine pregnancy test for females of childbearing potential.
- Confirm proper contraception is being used.
- Review changes in the subject's medical history including medication history since Screening.
- Perform [OST Examination-Edentulous](#).

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- Assess subject eligibility.
- Randomise subject to treatment group.
- Clean the subject's dentures using the supplied denture brush and cleansing paste, both the upper and lower dentures will be thoroughly cleaned to remove all traces of denture fixative, plaque and particulates/debris. Dentures should then be dried.
- Apply treatment and insert dentures per the [Product Application Instructions](#).
- 60±5 minutes after denture insertion, begin [Food Occlusion Testing including Denture Dislodgement Assessment](#).
- Record the number of denture dislodgements during peanut chewing.
- Subjects complete the questionnaire.
- Photograph dentures for a subset of subjects.
- Perform [OST Examination-Edentulous](#).
- Return clean dentures to subject.
- Record AEs and incidents. Assess symptoms by spontaneous reporting of adverse events and by asking the subjects to respond to a non-leading question such as "How do you feel?" Any adverse event that occurs subsequent to the first dose will be recorded.

6.1.3 Visit 3


Subjects will be admitted to the clinical site between 2-30 days after Visit 2. The following procedures will be completed in the following order (wherever possible) and recorded in the CRF:

- Review Inclusion and Exclusion criteria. Pregnancy status will be confirmed verbally by the subject.
- Collect urine pregnancy test for females of childbearing potential if required per [Section 7.3.2](#).
- Review changes in the subject's medical history including medication history since Screening.
- Perform [OST Examination-Edentulous](#).
- Assess subject eligibility.
- Clean the subject's dentures using the supplied denture brush and cleansing paste, both the upper and lower dentures will be thoroughly cleaned to remove all traces of denture fixative, plaque and particulates/debris. Dentures should then be dried.
- Apply treatment and insert dentures per the [Product Application Instructions](#).
- 60±5 minutes after denture insertion, begin [Food Occlusion Testing including Denture Dislodgement Assessment](#).
- Record the number of denture dislodgements during peanut chewing.
- Subjects complete the questionnaire.
- Photograph dentures for a subset of subjects.

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- Perform [OST Examination-Edentulous](#).
- Return clean dentures to subject.
- Record AEs and incidents. Assess symptoms by spontaneous reporting of adverse events and by asking the subjects to respond to a non-leading question such as “How do you feel?”

6.1.4 Visit 4

Subjects will be admitted to the clinical site between 2-30 days after Visit 3. The following procedures will be completed in the following order (wherever possible) and recorded in the CRF:

- Review Inclusion and Exclusion criteria. Pregnancy status will be confirmed verbally by the subject.
- Collect urine pregnancy test for females of childbearing potential if required per [Section 7.3.2](#).
- Review changes in the subject’s medical history including medication history since Screening.
- Perform [OST Examination-Edentulous](#).
- Assess subject eligibility.
- Clean the subject’s dentures using the supplied denture brush and cleansing paste, both the upper and lower dentures will be thoroughly cleaned to remove all traces of denture fixative, plaque and particulates/debris. Dentures should then be dried.
- Apply treatment and insert dentures per the [Product Application Instructions](#).
- 60±5 minutes after denture insertion, begin [Food Occlusion Testing including Denture Dislodgement Assessment](#).
- Record the number of denture dislodgements during peanut chewing.
- Subjects complete the questionnaire.
- Photograph dentures for a subset of subjects.
- Perform [OST Examination-Edentulous](#).
- Return clean dentures to subject.
- Record AEs and incidents. Assess symptoms by spontaneous reporting of adverse events and by asking the subjects to respond to a non-leading question such as “How do you feel?”
- Study conclusion.

If a subject has any clinically significant, study-related abnormalities at the conclusion of a scheduled inpatient portion of the study, the GSK CH medical monitor (or designated representative) should be notified and depending on the abnormality, the subject may be asked to remain at the clinical site until such abnormalities are deemed not clinically significant, or it is safe for outpatient follow-up. If the subject is unable or unwilling to remain at the clinical site and/or when outpatient follow-up is deemed appropriate, the GSK CH medical

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monitor (or designated representative) should be so notified, and the investigator should make every effort to arrange follow-up evaluations at appropriate intervals to document the course of the abnormalities.

6.2 Subject Withdrawal

At the end of the study subjects will be evaluated to determine if they completed all study procedures or if they were discontinued from the study early. If the subject discontinued at any point during the study, the primary reason for withdrawal should be recorded on the Study Conclusion page of the CRF by selecting one of the options below.

1. Subject did not meet study criteria
2. Adverse event
3. Subject lost to follow up
4. Protocol Violation
5. Withdrawal of informed consent
6. Other

Subjects may withdraw from the study at any time at their own request, or they may be withdrawn at any time at the discretion of the investigator or sponsor for safety or, behavioural reasons, or the inability of the subject to comply with the protocol-required schedule of study visits or procedures at a given study site.

The following circumstances require discontinuation of study treatment and/or premature subject withdrawal:

- Protocol violation that may impact the outcome of the subject's safety
- Withdrawal of informed consent
- Subject lost to follow-up
- Pregnancy
- Death


If a subject is discontinued or prematurely withdraws from the study, reasons for discontinuation or withdrawal and associated date must be documented in the relevant section(s) of the CRF.

If a subject does not return for a scheduled visit, every effort should be made to contact the subject. The Investigator or site staff should attempt to contact the subject twice. After two attempts, clinical site staff must send a registered letter. If no response is received from the subject, the subject will be considered lost to follow up. All attempts to contact the subject and information received during contact attempts must be documented in the CRF. In any circumstance, every effort should be made to document subject outcome, if possible. The

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investigator should inquire about the reason for withdrawal, request that the subject return for a final visit, if applicable, and follow-up with the subject regarding any unresolved AEs.

It may be appropriate for the subject to return to the clinical site for final safety assessments. Subjects should be questioned regarding their reason for withdrawal. An OST examination may be conducted at the investigator's discretion.

Lack of completion of all or any of the early termination procedures will not be viewed as protocol deviations so long as the subject's safety was preserved.

If the subject withdraws from the study and also withdraws consent for disclosure of future information, no further evaluations should be performed and no additional data should be collected. The sponsor may retain and continue to use any data collected before such withdrawal of consent.

7 ASSESSMENTS

Every effort should be made to ensure that protocol-required tests and procedures are completed as described. However, it is anticipated that from time to time there may be circumstances, outside the control of the investigator that may make it unfeasible to perform the test. In these cases, the investigator must take all steps necessary to ensure the safety and well-being of the subject. When a protocol-required test cannot be performed, the investigator will document the reason for the missed test and any corrective and preventative actions that he or she has taken to ensure that required processes are adhered to as soon as possible. The subject should continue in the study as long as the safety of the subject is not compromised. The study team must be informed of these incidents in a timely manner.

7.1 Screening

The following assessments will be performed at times defined in the [Study Procedures](#) section of this protocol.

7.1.1 Informed Consent

The investigator, or designee, must obtain written (signed and dated by the subject) informed consent from each subject participating in this study after adequate explanation of the aims, methods, objectives, and potential hazards of the study. The investigator, or designee, must also explain to the subjects that they are completely free to refuse to enter the study or to withdraw from it at any time. Appropriate forms for documenting a written consent will be provided by the investigator or by GSK CH. The investigator, or designee, should sign and date the consent form to confirm that the consent process was completed correctly. The subject, will be provided with a copy of their signed and dated consent form and any other written information which they should be instructed to retain. If, during a subject's participation in the study, any new information becomes available that may affect the subject's willingness to participate in the study, each ongoing subject should receive a copy of this new information and be re-consented into the study. Subjects will be provided with a

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copy of the signed and dated amended consent form. The date of consent will be recorded on the CRF.

7.1.2 Dental History

The Investigator, or medically qualified designee, will take a dental history from each subject. Dental history will include information of all prostheses in the mouth, maxillary and mandibular, as well as information regarding the age of the dentures, how long the subject has worn dentures, the prosthetic teeth material and whether the subject is a regular user of denture adhesives.

7.1.3 Well-Fit Assessment, Kapur (Olshan Modification) Index

Each denture (upper and lower) will be examined for retention and stability using the Kapur Index (Olshan Modification) ([Kapur, 1967](#); [Olshan, 1992](#)) by an examiner with expert knowledge of prosthodontics. A sum score (upper + lower) of ≥ 6 is required for inclusion.

Retention:

With gloved hands, the examiner will attempt to unseat the upper and lower denture by applying an opposing vertical force at the canine/lateral incisor region of the denture. The examiner will score **retention** as 0 - 5 using the following criteria:

- 5= Excellent- denture offers excellent resistance to vertical pull and lateral force.
- 4= Very Good- denture offers very good resistance to vertical pull and lateral force.
- 3= Good- denture offers moderate resistance to vertical pull and lateral force.
- 2= Fair- denture offers moderate resistance to vertical pull and little or no resistance to lateral forces.
- 1= Poor- denture offers slight resistance to vertical pull and little or no resistance to lateral force.
- 0= No retention- when the denture is seated in place, it displaces itself.

Stability:

With gloved hands, the examiner will attempt to rock the seated dentures by placing alternate horizontal force at the cuspid and contralateral molar regions of the upper and lower dentures. The examiner will score **denture stability** as 0 - 4 using the following criteria:

- 4= Excellent- when denture base offers no rocking on its supporting structures under pressure.
- 3= Good- when denture base has very slight rocking on its supporting structures under pressure.
- 2= Fair- when denture base has slight rocking on its supporting structures under pressure.
- 1= Poor- when denture base has moderate rocking on its supporting structures under pressure.
- 0= No stability- when denture base has extreme rocking under pressure.

Sum score (upper + lower denture) of <6 = dentures with poor retention and stability.

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Sum score (upper + lower denture) 6-9 = dentures with fair retention and stability.

Sum score (upper + lower denture) 10-14 = dentures with good retention and stability.

Sum score (upper + lower denture) >14 = dentures with very good retention and stability.

Subject recruitment will be controlled to ensure 50±10% of the subjects will be in each of the low and high Kapur-Olshan groups [the low Kapur-Olshan group is defined as a composite Kapur-Olshan score of 6-14 (clinically fair and good dentures) and the high Kapur-Olshan score as 15-18 (clinically very good dentures)].

7.1.4 Well Made Assessment

Clinical Acceptability

Each denture (upper and lower) will be examined. Only dentures having adequate (as judged by an examiner with expert knowledge of prosthodontics) vertical dimension, freeway space, horizontal occlusal relationships and border extension will be considered clinically acceptable. For each denture (upper and lower), the examiner will indicate acceptable or unacceptable on the CRF.

Denture Finish and Contour

The contour and finish of each denture (maxillary and mandibular) will be examined. Only dentures with acceptable (as judged by an examiner with expert knowledge of prosthodontics) porosity, tissue surfaces, polished surfaces, colour and thickness will be accepted. For each denture (upper and lower), the examiner will indicate acceptable or unacceptable on the CRF.

7.1.5 Food Migration Adequacy Determination


Subjects must complete the food migration adequacy assessment whilst using no denture adhesives/fixatives. Dentures should have been cleaned and dried by the study staff and replaced in the subject's mouth. Subjects will be provided with 30-32 grams (accurately weighed) of non-salted peanuts, divided into smaller portions of approximately eight peanut halves by the study staff. Each portion should be chewed by the subject for approximately 20 seconds, after which the subject will be instructed to swallow at anytime they are comfortable. Subjects will be allowed small sips of water during the peanut consumption to aid chewing as appropriate. After completion of the peanut consumption, the subject will rinse their mouth with water for five seconds before removing their denture. Subjects will be asked to remove their dentures (the examiner may assist in this if required) and place them into a labelled tray (with subject screening number) teeth side down, and may remove any residual peanut particles from their mouth with water and a gauze pad (not for collection). The amount of food particles on each denture will be visually assessed by the examiner according to the scale below and recorded in the CRF to determine if there is evidence of peanut particle migration under the dentures. The following 0 – 3 assessment scale will be used. Subjects who present no evidence of peanut particles under either the upper or lower denture (i.e. if either denture scores as 0) will not be eligible.

The location and extent of peanut particle migration will be rated as follows:

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0= None – No peanut migration under the denture.

1= Minimal – Slight migration of peanuts under the denture.

2= Moderate – Migration of peanuts over the internal walls of the denture.

3= Extensive – Peanuts migration on the crest of the denture.

Dentures should be cleaned thoroughly by the study staff prior to returning to the subject.

7.2 Efficacy

The following efficacy assessments will be performed at times defined in the [Study Procedures](#) section of this protocol.

7.2.1 Food Occlusion Testing Incorporating Denture Dislodgement Assessment

Food Occlusion will be measured by a trained or experienced operator using the method described below. 60±5 minutes after the dentures have been inserted:

1. The subject will be instructed to bite down firmly on their dentures. The subject will then briefly rinse their mouth vigorously with water. The site staff will remove any adhesive that is oozing from the dentures. Note: The subject must not eat any food during the 60±5 minutes waiting period. Subjects may not drink during this 60±5 minutes period with the exception of small sips water.
2. The subject will be given 30-32g of non-salted, dry roasted peanuts to chew and swallow. The 32g portion of peanuts will be divided by the site staff in to smaller portions of approximately 8 peanut halves (approximately 4g). The subject will be asked to chew each pre-measured portion of peanuts for at least 20 seconds, after which they may swallow at any time they are comfortable. The subject may sip water during peanut consumption.
3. Whilst consuming the peanuts the subject should note the number of times they experience their denture dislodging. The total number of denture dislodgements for the subject should be recorded by the study site staff in the CRF.
4. After consuming all of the peanuts, the subject will rinse their mouth with water for approximately 5 seconds (to remove any peanut particles not retained under the dentures).
5. The examiner will carefully remove the subject's lower denture and place it on a small tray, teeth side down and remove any residual adhesive and/or peanut particles from the lower gum with a piece of gauze that will be placed in a separate beaker coded with the subject screening number, treatment period and "L" for lower denture.
6. The examiner will carefully remove the subject's upper denture and place it on a small tray, teeth side down and remove any residual adhesive and/or peanut particles from the roof of the mouth with a piece of gauze that will be placed in a separate beaker coded with the subject screening number, treatment period and "U" for upper denture.

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7. All the surfaces of the dentures will be checked for residual peanuts. If any is found on any surface other than those in contact with oral soft tissue, it will be removed with a spatula and discarded.
8. For a subset of approximately 5 subjects at each treatment visit, a photograph of the fit surface of the dentures will be taken as per section 7.2.3.
9. The upper and lower dentures of each subject will be placed in the coded beakers with the gauze (upper and lower separately).
10. Immediately following removal of the prostheses the subject will complete the study questionnaire per section 7.2.2.
11. In the laboratory, approximately 100 ml (or enough to cover the prostheses) of hot de-ionised water (90 °C, (194 °F)) will be added to each beaker. The beakers will be sonicated for 30 minutes to loosen any adhering peanut particles.
12. After sonication, any peanut particles still remaining on the prostheses or the gauze will be washed out into the beaker. The gauze pieces will be discarded and the dentures will be cleaned and returned to the subject.
13. The dentures should be cleaned thoroughly before returning to the subject.
14. The solutions in the beakers (mixture of water, adhesive, saliva and peanut particles) will be heated to boiling with frequent stirring to dissolve any undissolved adhesive.
15. The hot solution in each beaker will be strained through a standard testing sieve, USA #60 (coded with subject's screening number, treatment code and U or L for upper and lower dentures).
16. The residue remaining on the screen will be washed repeatedly with hot water to remove any adhesive or saliva.
17. The collected peanut particles will be air-dried overnight on the screen.
18. The dried particles will be transferred from the screen to pre-weighed coded (subject screening number, Upper/Lower and date) aluminium weighing pans using a spatula and then will be dried in an oven at 40°C (105°F) for 5 hours.
19. The pans will be removed from the oven, cooled to room temperature and then weighed (in grams, to 4 decimal places) to determine the mass of the particles collected from each denture.

Prior to commencing this testing the subjects will have the entire food occlusion and denture dislodgement assessment procedure explained to them at each visit by the examiner or a designee. A standard script will be used to ensure consistency in procedures.

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7.2.2 Subject Questionnaire

After the food occlusion testing and following removal of the dentures on Test Days, the subject will complete a questionnaire ([Section 13.2](#)) on their experience during the chewing procedure. The subject responses should be transcribed by the study staff to the CRF. The study staff should be mindful that whilst the questionnaire does not solicit safety information, any information on safety outcomes recorded by subjects on the questionnaire should be evaluated by the investigator to ensure all AEs are recorded.

7.2.3 Denture Photographs at Treatment Visits

For a subset of subjects, extra oral digital photographs will be taken of the underside of each denture immediately after their removal to document the appearance of migrated particles for sponsor review. Subjects will be selected at the discretion of the Investigator, but allow for a variety of denture sizes and fit to be represented. It is expected that approximately 5 sets of dentures be photographed per treatment group, and where possible that consistency of subjects between treatments is maintained (i.e. a subject will be identified at visit 2 as being suitable for denture imaging and will have their dentures photographed at visit 2, 3 and 4). Should subject dropouts or other reasons necessitate, subjects can be substituted. Digital photographs and their filenames should not contain any personally identifiable information. The digital file should be appropriately named to identify the subject screening number and the treatment period. This procedure should be undertaken by the examiner or designee.

7.3 Safety

The following safety assessments will be performed at times defined in the [Study Procedures](#) section of this protocol.


7.3.1 Oral Soft Tissue (OST) Examination - Edentulous

The OST examination should be performed by a qualified dentist and ideally the same examiner should be used. The OST Exam-Edentulous will include the labial mucosa (including lips), buccal mucosa, tongue, gingival mucosa, sublingual area, hard and soft palates, mucogingival folds, submandibular area, salivary glands, tonsillar and pharyngeal areas. Observations will be made of any erythema, desquamation and ulcerations, and other relevant clinical observations. The results of the examination will be recorded in the CRF as either normal or abnormal. The location and brief description of any abnormalities will also be recorded.

7.3.2 Pregnancy Testing

For female subjects of childbearing potential, a urine pregnancy test, will be performed at Visit 2 and then again at Visits 3 and 4 in the event that more than 30 days have elapsed since their previous Pregnancy test. Results will be obtained prior to dosing during each period.

A negative pregnancy result is required before the subject may receive the investigational product. Pregnancy tests will also be done whenever one menstrual cycle is missed during the

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active study period (or when potential pregnancy is otherwise suspected). Pregnancy tests may also be repeated as per request of IRBs/ECs or if required by local regulations.

In the case of a positive confirmed pregnancy, the subject will be withdrawn from administration of investigational product and from the study.

If a urine sample is collected as part of the pregnancy testing it will be disposed of immediately after the conclusion of the test

8 ADVERSE EVENT AND OTHER EVENTS OF SPECIAL INTEREST REPORTING

8.1 Definitions of Adverse Events and Serious Adverse Events

8.1.1 Adverse Event

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of an investigational or washout product or medical device, whether or not considered related to the investigational or washout product or medical device.

NOTE: An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study treatment.

Events Meeting the AE Definition:

- Any abnormal safety assessments (e.g., OST findings, including those that worsen from baseline, considered clinically significant in the medical and scientific judgment of the investigator (ie, not related to progression of underlying disease)).
- Exacerbation of a chronic or intermittent pre-existing condition including either an increase in frequency and/or intensity of the condition.
- New conditions detected or diagnosed after study treatment administration even though it may have been present before the start of the study.
- Signs, symptoms, or the clinical sequelae of a suspected drug-drug interaction.
- Signs, symptoms, or the clinical sequelae of a suspected overdose of either study treatment or a concomitant medication. Overdose per se will not be reported as an AE/SAE unless it is an intentional overdose taken with possible suicidal/self-harming intent. Such overdoses should be reported regardless of sequelae.
- "Lack of efficacy" or "failure of expected pharmacological action" *per se* will not be reported as an AE or SAE. Such instances will be captured in the efficacy assessments. However, the signs, symptoms, and/or clinical sequelae resulting from lack of efficacy will be reported as AE or SAE if they fulfil the definition of an AE or SAE.

Events NOT meeting the AE definition:

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- Any clinically significant abnormal laboratory findings (if applicable) or other abnormal safety assessments which are associated with the underlying disease, unless judged by the investigator to be more severe than expected for the subject's condition.
- The disease/disorder being studied or expected progression, signs, or symptoms of the disease/disorder being studied, unless more severe than expected for the subject's condition.
- Medical or surgical procedure (e.g., endoscopy, appendectomy) is not the AE. The condition that leads to the procedure is an AE (e.g., appendicitis).
- Situations where an untoward medical occurrence did not occur (social and/or convenience admission to a hospital).
- Anticipated day-to-day fluctuations of pre-existing disease(s) or condition(s) present or detected at the start of the study that do not worsen.

8.1.2 Serious Adverse Event

If an event is not an AE per definition above, then it cannot be an SAE even if serious conditions are met (e.g., hospitalisation for signs/symptoms of the disease under study, death due to progression of disease).

A serious adverse event is any untoward medical occurrence at any dose that:

- **Results in death**
- **Is life-threatening**
 - The term 'life-threatening' in the definition of 'serious' refers to an event in which the participant was at risk of death at the time of the event. It does not refer to an event, which hypothetically might have caused death, if it were more severe;
- **Requires inpatient hospitalisation or prolongation of existing hospitalisation**
 - In general, hospitalisation signifies that the participant has been detained (usually involving at least an overnight stay) at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician's office or outpatient setting. Complications that occur during hospitalisation are AE. If a complication prolongs hospitalisation or fulfils any other serious criteria, the event is serious. When in doubt as to whether "hospitalisation" occurred or was necessary, the AE should be considered serious.
 - Hospitalisation for elective treatment of a pre-existing condition that did not worsen from baseline is not considered an AE.
- **Results in persistent or significant disability/incapacity**
 - The term disability means a substantial disruption of a person's ability to conduct normal life functions.
 - This definition is not intended to include experiences of relatively minor medical significance such as uncomplicated headache, nausea, vomiting, diarrhoea,

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influenza, and accidental trauma (e.g., sprained ankle) which may interfere with or prevent everyday life functions but do not constitute a substantial disruption

- **Results in congenital anomaly/birth defect**
- **Other situations**
 - Medical or scientific judgment should be exercised in deciding whether SAE reporting is appropriate in other situations such as important medical events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardize the participant or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These events should usually be considered serious.
 - Examples of such events include invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalisation, or development of drug dependency or drug abuse.

8.2 Reporting Period

8.2.1 Adverse Event

AEs will be collected from the first use of investigational treatment at Visit 2 and until 5 days following last administration of treatment.

Medical occurrences that begin before the start of study treatment but after obtaining informed consent will be recorded on the Medical History/Current Medical Conditions section of the case report form (CRF) not the AE section.

8.2.2 Serious Adverse Event

SAEs assessed as **related** to study participation (e.g., investigational product, protocol mandated procedures, invasive tests, or change in existing therapy) or related to a GSK concomitant medication will be recorded from the time a subject provides informed consent, which is obtained prior to the subject's participation in the study, i.e., prior to undergoing any study-related procedure and/or receiving investigational product and until 5 days following last administration of the investigational product.

SAEs assessed as **not related** to study participation (e.g., investigational product, protocol mandated procedures, invasive tests, or change in existing therapy) or not related to a GSK concomitant medication will be recorded from the time the subjects provides informed consent and until 5 days following last administration of the investigational product.


8.3 Reporting Procedures

The investigator and any designees are responsible for detecting, documenting and reporting events that meet the definition of an AE or SAE and remain responsible for following up on AEs that are serious, considered related to the study treatment or the study, or that caused the participant to discontinue the study treatment.

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The investigator is to report all directly observed AEs and all AEs spontaneously reported by the study subject. In addition, each study subject will be questioned about AEs.

Each AE is to be assessed to determine if it meets the criteria for SAEs. If an SAE occurs, expedited reporting will follow local and international regulations, as appropriate.

When an AE/SAE occurs, it is the responsibility of the investigator to review all documentation (e.g., hospital progress notes, laboratory, and diagnostics reports) related to the event.

The investigator or site staff will then record all relevant information regarding an AE/SAE in the CRF.

It is **not** acceptable for the investigator to send photocopies of the participant's medical records to GSK in lieu of completion of the GSK /AE/SAE CRF page.

There may be instances when copies of medical records for certain cases are requested by GSK. In this instance, all subject identifiers, with the exception of the subject number, will be blinded on the copies of the medical records prior to submission to GSK.

The investigator will attempt to establish a diagnosis of the event based on signs, symptoms, and/or other clinical information. In such cases, the diagnosis will be documented as the AE/SAE and not the individual signs/symptoms. Clinical AEs will be described by diagnosis and not by symptoms when possible (e.g., upper respiratory tract infection, seasonal allergy, etc. instead of runny nose).

Medical conditions reported prior to the time period for reporting AEs/SAEs should be recorded as part of the subject's medical history.

AEs elicited by the investigator in a standard manner at the study visits should also be recorded in the AE section of the CRF. Care will be taken not to introduce bias when detecting AE and/or SAE. Open-ended and non-leading verbal questioning of the participant is the preferred method to inquire about AE occurrence.


8.3.1 Adverse Event

All AEs will be reported on the AE page(s) of the CRF by the investigator or site staff. It should be noted that the form for collection of SAE information is not the same as the AE CRF. Where the same data are collected, the forms must be completed in a consistent manner. For example, the same AE term should be used on both forms. AE should be reported using concise medical terminology on the CRF as well as on the form for collection of SAE information.

8.3.2 Serious Adverse Event

A paper copy of the SAE form provided in the investigator study master file should be completed as fully as possible.

It is essential to enter the following information:

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- Protocol and subject identifiers
- Subject's demography
- Description of events, with diagnosis if available
- Investigator opinion of relationship to study product
- Criterion for seriousness.

The following are desirable and are of particular relevance for investigator and GSK CH assessment of the SAE report:

- Date of onset of AE
- Date AE stopped, if relevant
- Study product start date
- Study product end date if relevant
- Action taken on study product
- Outcome if known

The SAE form, completed as fully as possible, must be e-mailed to the GSK CH Clinical Operations Safety Reporting email box with the study number and subject number in the subject line of the email **immediately and under no circumstance should this exceed 24 hours** after study site personnel learn of the event. The investigator will submit any updated SAE data to the sponsor, **immediately and under no circumstance should this exceed 24 hours** of it being available. The GSK CH Study Manager should also be notified of the situation by telephone or email.

Email Serious Adverse Events to:

PPD

The GSK CH Study Manager or designee will be responsible for forwarding the SAE form to the Case Management Group, Global Clinical Safety and Pharmacovigilance mailbox
PPD

The initial report will be followed up with more information as relevant, or as requested by the GSK CH study manager.

8.3.3 Sponsor's Reporting Requirements to Regulatory Authorities and Ethics Committees

GSK has a legal responsibility to notify, as appropriate, the local regulatory authority and other regulatory authorities about the safety of a product under clinical investigation. Prompt

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notification of SAEs by the investigator to GSK is essential so that legal obligations and ethical responsibilities towards the safety of subjects are met.

GSK will comply with country specific regulatory requirements relating to safety reporting to the regulatory authority, IRB/EC and investigators.

Investigator safety reports must be prepared for suspected unexpected serious adverse reactions (SUSAR) according to local regulatory requirements and sponsor policy and forwarded to investigators as necessary.

An investigator who receives an investigator safety report describing a SAE or other specific safety information e.g., summary or listing of SAE) from the sponsor will review and then file it along with the Investigator's Brochure and will notify the IRB/IEC, if appropriate according to local requirements.

8.4 Evaluating Adverse Events and Serious Adverse Events

8.4.1 Severity Assessment

The investigator or designee will make an assessment of severity for each AE and SAE reported during the study and will assign it to one of the following categories:


- **Mild:** An event that is easily tolerated by the subject, causing minimal discomfort and not interfering with everyday activities.
- **Moderate:** An event that is sufficiently discomforting to interfere with normal everyday activities
- **Severe:** An event that prevents normal everyday activities.

Note: An AE that is assessed as severe will not be confused with an SAE. Severity is a category utilised for rating the intensity of an event; and both AEs and SAEs can be assessed as severe. For example, a headache may be severe (interferes significantly with the subject's usual function) but would not be classified as serious unless it met one of the criteria for SAEs, listed above.

8.4.2 Causality Assessment

The causality assessment is one of the criteria used when determining regulatory reporting requirements. For each AE/SAE, the investigator **must** document in the medical notes that he/she has reviewed the AE/SAE and has provided an assessment of causality. The investigator's assessment of causality must be provided for all AEs (serious and non-serious); the investigator must record the causal relationship in the CRF, as appropriate, and report such an assessment in accordance with the SAE reporting requirements if applicable.

A "reasonable possibility" of a relationship conveys that there are facts, evidence, and/or arguments to suggest a causal relationship, rather than a relationship cannot be ruled out. Generally, the facts (evidence) or arguments to suggest a causal relationship should be provided.

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The investigator will use clinical judgment to determine the relationship and will also consult the Investigator Brochure (IB), Safety Statement and/or Product Information, for marketed products, in the determination of his/her assessment. Alternative causes, such as underlying disease(s), concomitant therapy, other risk factors, and the temporal relationship of the event to the study product will be considered and investigated.

There may be situations when an SAE has occurred and the investigator has minimal information to include in the initial report to GSK. However, it is very important that the investigator always make an assessment of causality for every event prior to the initial transmission of the SAE data to GSK. The investigator may change his/her opinion of causality in light of follow-up information and send an SAE follow-up report with the updated causality assessment.

8.5 Withdrawal Due to an Adverse Event and Serious Adverse Events

Withdrawal due to AEs should be distinguished from withdrawal due to other causes, according to the definition of AE noted earlier, and recorded on the appropriate AE CRF page.

When a subject withdraws because of an SAE, the SAE must be reported in accordance with the reporting requirements defined below.

8.6 Pregnancy

8.6.1 Time Period for Collecting Pregnancy Information

Pregnancy information will be collected on all pregnancies reported following administration of any investigational product or washout product and until 5 days following last administration of the investigational product.

8.6.2 Action to be Taken if Pregnancy Occurs

The investigator will collect pregnancy information on any subject who becomes pregnant while participating in the study after administration of the investigational product or washout product. The investigator will record pregnancy information on the appropriate form and e-mail it to the GSK CH Clinical Operations Safety Reporting email box ^{PPD}

within 24 hours of learning of the subject becoming pregnant. The GSK CH Study Manager or designee will be responsible for forwarding the SAE form to the Case Management Group, Global Clinical Safety and Pharmacovigilance mailbox ^{PPD}

The subject will be followed to determine the outcome of the pregnancy. Information on the status of the mother and infant / neonate (including concomitant medications taken by the mother during the pregnancy) will be forwarded by the investigator to the GSK CH Clinical Operations Safety Reporting email box and the GSK CH Study Manager or designee will forward this information to the Case Management Group, Global Clinical Safety and

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Pharmacovigilance group mailbox at GSK PPD. Generally, follow-up will be no longer than 6 to 8 weeks following the estimated delivery date. Any termination of the pregnancy will be reported.

While pregnancy itself is not considered to be an AE, abnormal pregnancy outcomes (eg, spontaneous abortion, foetal death, stillbirth, congenital anomalies, ectopic pregnancy) are considered to be and should be recorded as an SAE.

Any female participant who becomes pregnant while participating will be withdrawn from the study.

8.7 Follow-up of Adverse Events and Serious Adverse Events

After the initial report, the investigator is required to proactively follow up with each subject and provide further information on the subject's condition.

All AEs/SAEs will be followed until resolution, until the condition stabilises, until the event is otherwise explained, or until the subject is lost to follow-up.

The investigator is obligated to perform or arrange for the conduct of supplemental measurements and/or evaluations as may be indicated or as requested by GSK to elucidate as fully as possible the nature and/or causality of the AE or SAE. This may include additional laboratory tests or investigations, histopathological examinations, or consultation with other health care professionals.

New or updated information will be recorded in the originally completed CRF.

The investigator will submit any updated SAE data to GSK within 24 hours of receipt of the information.

Investigators are not obliged to actively seek AEs or SAEs in former subjects. However, if the investigator learns of any SAE, including the death, at any time after a subject has been discharged from the study, and considers the event reasonably related to the investigational product or study participation, the investigator will promptly notify GSK by emailing the information to the GSK CH Clinical Operations Safety Reporting email box PPD. The GSK CH Study Manager or designee will be responsible for forwarding the information to the Case Management Group, Global Clinical Safety and Pharmacovigilance group mailbox at GSK PPD.

The investigator will submit any updated SAE data to GSK within the designated reporting time frames.

8.8 Definition of and Procedure for Reporting Medical Device Incidents

Medical devices are being provided by GSK CH for use in this study namely the Test Denture Adhesive, the denture brushes and the denture cleansing paste.

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8.8.1 Definition of an Incident

A medical device incident is any malfunction or deterioration in the characteristics and/or performance of a device as well as any inadequacy in the labelling or the instructions for use which, directly or indirectly, might lead to or might have led to the death of a participant/user/other person or to a serious deterioration in his/her state of health.

Not all incidents lead to death or serious deterioration in health. The non-occurrence of such a result might have been due to other fortunate circumstances or to the intervention of health care personnel.

It is sufficient that:

- An incident associated with a device happened and
- The incident was such that, if it occurred again, might lead to death or a serious deterioration in health.

A serious deterioration in state of health can include any of the following:


- Life-threatening illness
- Permanent impairment of body function or permanent damage to body structure
- Condition necessitating medical or surgical intervention to prevent one of the above
- Foetal distress, foetal death, or any congenital abnormality or birth defects

Examples of incidents:

- A participant, user, caregiver, or healthcare professional is injured as a result of a medical device failure or its misuse.
- A participant's study treatment is interrupted or compromised by a medical device failure.
- A misdiagnosis due to medical device failure leads to inappropriate treatment.
- A participant's health deteriorates due to medical device failure.

8.8.2 Reporting of an Incidents and Malfunctions

- All incidents must be reported to GSK within 24 hours (or sooner if possible) of the investigator or designee becoming aware of the situation.
- Any medical device incident occurring during the study will be documented in the subject's medical records, in accordance with the investigator's normal clinical practice, and on the appropriate Incident Report Form. In addition, for incidents fulfilling the definition of an AE or an SAE, the appropriate AE CRF page or SAE form will be completed and reported as per the AE and SAE reporting sections.

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- The Incident Report Form will be completed as thoroughly as possible and signed by the investigator before transmittal to GSK CH. It is very important that the investigator describes any corrective or remedial actions taken to prevent recurrence of the incident.
- The completed Incident Report Form should be emailed to the GSK CH Clinical Operations Safety Reporting email box with the study number and subject number in the subject line of the email as soon as possible, **but not later than 24 hours** after study site personnel learn of the event. If there is an SAE, the completed SAE pages should be sent together with this report form. However, if a copy of the SAE report is sent with this form, this does not replace the procedure to report an SAE. The original Incident Report Form will remain with the subject's records.
- The GSK CH Study Manager should be notified of the situation by telephone or email.

Email the Incident Report Forms to:

PPD

- The GSK CH Study Manager or designee will be responsible for forwarding the Incident Report Form to the Case Management Group, Global Clinical Safety and Pharmacovigilance group mailbox PPD, responsible for the study and other GSK CH personnel as appropriate.
- The initial report will be followed up with more information as relevant, or as requested by the GSK CH study manager.

The investigator will follow the following directions regarding the reporting of a device failure (malfunction):

- Notify GSK CH immediately (by following the process described above).
- Schedule the subject to return to the site promptly to return the failed device.
- Record any incidents on the CRF and Incident Report Form following instructions given in the section above.
- Return the failed device to the sponsor as soon as possible, including documentation of the details of the failure


8.8.3 Follow-up of Medical Device Incidents

- All medical device incidents involving an AE will be followed and reported in the same manner as other AEs. This applies to all participants, including those who discontinue study treatment or the study.
- The investigator is responsible for ensuring that follow-up includes any supplemental investigations as indicated to elucidate the nature and/or causality of the incident.
- New or updated information will be recorded on the originally completed form with all changes signed and dated by the investigator.

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8.8.4 Regulatory and Ethics Reporting Requirements for Incidents

- In order to fulfil regulatory reporting obligations worldwide, the investigator is responsible for the detection and documentation of events meeting the definitions of incident or malfunction that occur during the study with such devices. Medical device incidents or malfunctions of the device that result in an incident will be detected, documented, and reported during all periods of the study in which the medical device is used.
- The investigator will promptly report all incidents occurring with any medical device provided for use in the study in order for the sponsor to fulfil the legal responsibility to notify appropriate regulatory authorities and other entities about certain safety information relating to medical devices being used in clinical studies.
- The investigator, or responsible person according to local requirements (e.g., the head of the medical institution), will comply with the applicable local regulatory requirements relating to the reporting of incidents to the IRB/IEC.

9 DATA MANAGEMENT

As used in this protocol, the term CRF should be understood to refer to either a paper form or an electronic data record or both, depending on the data collection method used in this study.

For this study subject data will be entered into an electronic CRF, using a validated system.

9.1 Source Documents/ Data

The source documents (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files and records kept at the pharmacy, at the laboratory and at the medico-technical departments involved in the clinical study) which contain the source of data recorded in the CRF should be specified in Section 6 . The CRF can be used as a source document at the discretion of data management.

Each subject will be assigned and identified by a unique Number. Any reference made to an individual subject within the study must be done using the unique Screening Number.

9.2 Case Report Form

A CRF is a printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial subject.

For each subject who has given informed consent/assent and has been screened, CRF must be completed and signed by the Principal Investigator (or authorised designee) to certify that the data are complete and correct.

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Management of clinical data will be performed in accordance with Third Party BDM Vendor applicable standards and data cleaning procedures with oversight by GSK CH to ensure integrity of the data e.g., removing errors and inconsistencies in the data.

In order to protect the privacy of subjects, no Personally Identifiable Information (PII) (including the subject's name or initials or full birth date) is to be recorded in the CRF or as part of the query text.

All CRF pages should be completed during a subject assessment when the CRF has been designated as the source. Data that is sourced elsewhere should be entered into the CRF in an agreed upon timeframe between the Investigator and Sponsor.

GSK CH will obtain and retain all CRFs and associated study data at the completion of the study.

9.3 Data Handling

Documentation of all data management activities should allow step-by-step retrospective assessment of data quality and study performance.

Any changes or corrections to data will be performed in the Electronic Data Capture (EDC) System, and it will include rationale for changes. The EDC system has an audit trail, which will provide a complete record of the changes and corrections endorsed by the Investigator.

Any corrections to the entries made to paper source documents must be dated, initialled, and explained (if necessary) and should not obscure the original entry.

Adverse events will be coded using MedDRA (Medical Dictionary for Regulatory Activities) and concomitant medications terms (if applicable) using an internal validated medication dictionary, GSKDrug.

9.3.1 Queries

Programmed edit checks will be generated automatically, as the data is being entered into the system. Data Management will also run reports and listings on the CRF data, in addition to the queries already programmed and generated by the system, to raise manual queries as needed for site clarification or correction. The Clinical Dictionary Development and Management Group will raise queries as needed on safety data to code the terms (Adverse Events and Drugs) appropriately.

The study monitor at the study site will review the CRFs in accordance with the monitoring plan, and any queries will be generated in the EDC System to the Investigator or designee, enabling the errors to be addressed in parallel with Data Management review. The study monitor can also run reports and listings on the CRFs, to raise manual queries as needed for site clarification or correction.


9.4 Processing Patient Reported Outcomes

Patient reported outcome (PRO) data may be collected from diary cards, questionnaires, etc, and entered into the sponsor's clinical data management system (DMS). In instances where

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the PRO data is entered into the DMS by GSK CH, the PROs will be anonymised as agreed and documented prior to study initiation. PROs that are source will be retained by the investigator and certified copies will be sent to GSK CH.

In order to protect the privacy of subjects, no Personally Identifiable Information (PII) (including the subject's name or initials or birth date) is to be recorded on all PRO's that will be forwarded to GSK CH.

All PRO source data should be reviewed by the study staff/study monitor (as appropriate) to ensure that any potential AEs reported on these documents are represented in the DMS.

9.5 External Data

External Data are subject data obtained externally to the CRF. These data are generated from laboratory instruments, computers or other sources and then transcribed into a file and format agreed upon by GSK CH to identify the subject and time point referenced in the CRF and/or protocol.

An agreed upon quality control process is performed against the transcribed data to the source to ensure the accuracy of the transcription. The transcribed data is transmitted in an agreed upon format to GSK CH.

Reconciliation will be performed between the transcribed data and the clinical database to ensure subject and time point referenced in the Clinical Database match before Clinical Database Freeze (locking of the database) can occur.

10 STATISTICAL CONSIDERATIONS AND DATA ANALYSES

10.1 Sample Size Determination

Since this is an exploratory methodology development study, no formal sample size calculation was conducted. CCI

Therefore, approximately 48 (maximum 50) healthy subjects with both maxillary and mandibular full dentures will be enrolled in this study. Subject recruitment will be controlled to ensure 50±10% of the subjects will be in each of the low and high Kapur-Olshan groups [the low Kapur-Olshan group is defined as a composite Kapur-Olshan score of 6-14 (clinically fair and good dentures) and the high Kapur-Olshan score as 15-18 (clinically very good dentures)].

10.2 Statistical Methods and Analytical Plan

Additional details of the proposed statistical analysis will be documented in the statistical analysis plan (SAP), which will be written following finalisation of the protocol and prior to study unblinding / analysis (as appropriate).

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10.2.1 Definition of Analysis Populations

- All assessments of safety will be based on the safety population, defined as all subjects who are randomised and receive at least one dose of study treatment during the study. Safety population summaries will be presented by treatment received.
- The primary population for efficacy assessment will be the intent-to-treat (ITT) population, defined as all subjects who are randomised, receive the study treatment at least once and provide at least one assessment of efficacy.
- The PP population includes all subjects who fully comply with all study procedures and restrictions.

10.2.2 Exclusion of Data from Analysis

Exclusion of any data from the analyses will be determined during a Blind Data Review Meeting prior to database lock. Any reasons for exclusion from an analysis population will be listed, if applicable.

The Per Protocol (PP) population will be a subset of the ITT population.

Subjects with a protocol violation that is deemed to affect efficacy for all efficacy assessments will be excluded from the PP population. Subjects with a protocol violation that is deemed to affect efficacy for only some (but not all) of the efficacy assessments will be part of the PP population, but their data will be excluded from the assessment at which the protocol violation occurred. A PP analysis will be performed only if 10% or more ITT subjects are excluded from PP population.

10.2.3 Demographic and Baseline Characteristics

Descriptive statistics (number of subjects, mean, standard deviation, median, minimum and maximum for continuous variables, and frequency and percentage for categorical variables) will be provided for demographic and baseline characteristics. Medical history and current medical conditions will be listed.

10.2.4 Treatments (study drug/product, rescue medication, other concomitant therapies, compliance)

Prior medications, concomitant medications and significant non-drug therapies taken during treatment will be listed for the safety population. Compliance to the study products will also be summarised.

10.2.5 Primary Analysis

Food occlusion will be measured by weight of peanut particles (mass of retrieved peanuts in grams). Descriptive statistics (Raw means, standard deviations, standard errors, minimum and maximum values) of combined masses of peanuts recovered from mandibular and maxillary dentures and their associated gauzes will be provided by treatment group.

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10.2.6 Safety Analysis

All AEs will be coded using MedDRA. AEs will be categorised as oral and non-oral by the Clinical Research Director/ Scientist or designee prior to database lock. Treatment-emergent adverse event (Oral AEs as well as all AEs) will be associated with the most recent treatment received. The number of AEs and number of subjects with AEs will be listed and tabulated by treatment. The results of OST exams will be listed. Incidents will be listed.

10.2.7 Other Analyses

Descriptive statistics (Raw means, standard deviations, standard errors, minimum and maximum values) of masses of peanuts recovered from mandibular, maxillary and combined dentures will be provided by treatment group.

Descriptive statistics (Raw means, standard deviations, standard errors, minimum and maximum values) of combined masses of peanuts recovered from mandibular and maxillary dentures will be provided by treatment group in low and high Kapur-Olshan groups of subjects.

Descriptive statistics (Raw means, standard deviations, standard errors, minimum and maximum values) will also be provided for the number of denture dislodgements by treatment group. Mass of peanuts will also be plotted against the number of dislodgements overall and by treatment group.

For the subjects' responses to questionnaires, descriptive statistics (number of subjects and percentages) will be provided for each question by treatment group.

10.2.8 Additional Analyses


For future development work, adjusted means of masses of peanuts recovered from mandibular, maxillary and combined dentures, along with 95% confidence interval will also be reported by treatment group. These will be derived from a mixed model with period and treatment as fixed effects and subject as a random effect. Treatment differences and 95% confidence intervals of treatment differences will be reported.

Using the same model as above, a subgroup analysis will be also conducted in low and high Kapur-Olshan groups of subjects. Adjusted means of combined masses of peanuts recovered from mandibular and maxillary denture, along with 95% confidence interval will be reported by treatment groups for each sub-group.

These results will be reported in the statistical appendix as part of the CSR.

10.2.9 Handling of Dropouts and Missing Data

Subjects who withdraw from the study early will be included in the study analysis up to the point of withdrawal. Subjects who withdraw will not be replaced. No data will be imputed in the case of dropouts or missing data.

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10.2.10 Interim Analysis

No interim analysis is planned for this study.

11 STUDY GOVERNANCE CONSIDERATIONS

11.1 Quality Control

In accordance with applicable regulations including GCP, and GSK procedures, GSK or designee (i.e. third party vendor) monitors will contact the site prior to the start of the study to review with the site staff the protocol, study requirements, and their responsibilities to satisfy regulatory, ethical, and GSK requirements.

When reviewing data collection procedures, the discussion will include identification, agreement and documentation of data items for which the CRF will serve as the source document.

GSK or designee will monitor the study and site activity to verify that the:

- Data are authentic, accurate, and complete.
- Safety and rights of subjects are being protected.
- Study is conducted in accordance with the currently approved protocol and any other study agreements, GCP, and all applicable regulatory requirements.

The extent and nature of monitoring will be described in a written monitoring plan on file at GSK CH. The investigator (or designee) agrees to allow the monitor direct access to all relevant documents and agrees to co-operate with the monitor to ensure that any problems detected in the course of these monitoring visits are resolved.

11.2 Quality Assurance

To ensure compliance with GCP and all applicable regulatory requirements, GSK may conduct a quality assurance assessment and/or audit of the site records, and the regulatory agencies may conduct a regulatory inspection at any time during or after completion of the study.

In the event of an assessment, audit or inspection, the investigator (and institution) must agree to grant the advisor(s), auditor(s) and inspector(s) direct access to all relevant documents and to allocate their time and the time of their staff to discuss the conduct of the study, any findings/relevant issues and to implement any corrective and/or preventative actions to address any findings/issues identified.

The investigator(s) will notify GSK CH or its agents immediately of any regulatory inspection notification in relation to the study. Furthermore, the investigator will cooperate with GSK CH or its agents to prepare the study site for the inspection and will allow GSK CH or its agent, whenever feasible, to be present during the inspection. The investigator will promptly apply copies of the inspection finding to GSK CH or its agent. Before response submission to

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the regulatory authority, the investigator will provide GSK CH or its agents with an opportunity to review and comment on responses to any such findings.

The sponsor will be available to help investigators prepare for an inspection.

11.3 Regulatory and Ethical Considerations

As per the Regulatory Determination for this study, the denture adhesive product to be used in this study is already marketed in the US. The study is not intended to assess safety and efficacy, though safety is a secondary objective in that treatment emergent AEs will be collected, as per any clinical study. We do not anticipate any risk associated with the use of the syringe for adhesive application instead of applying directly from tube as done for the marketed product. As such, this study is an IDE exempt medical device study as per 21 CFR 812.2(c)(1) and 21 CFR 812.2(c)(4). This study does not require regulatory approval prior to conducting the study.

11.3.1 Institutional Review Board

It is the responsibility of the investigator to have prospective approval of the study protocol, protocol amendments, informed consent documents, safety statement (including any updates) and other relevant documents, e.g., recruitment advertisements, if applicable, from the IRB. All correspondence with the IRB should be retained in the investigator file. Copies of IRB approvals should be forwarded to GSK CH prior to the initiation of the study, and also when subsequent amendments to the protocol are made.

The only circumstance in which an amendment may be initiated prior to IRB approval is where the change is necessary to eliminate apparent immediate hazards to the subjects. In that event, the investigator must notify the IRB and GSK CH in writing immediately after the implementation.

11.3.2 Ethical Conduct of the Study

The study will be conducted in accordance with legal and regulatory requirements, as well as the general principles set forth in the International Ethical Guidelines for Biomedical Research Involving Human Subjects (Council for International Organizations of Medical Sciences 2002), guidelines for GCP (([ICH, 1996](#)) and revision 2), and the Declaration of Helsinki (([World Medical Association, 2008](#))).

In addition, the study will be conducted in accordance with the protocol, the ICH guideline on GCP, and applicable local regulatory requirements and laws.

11.3.3 Subject Information and Consent

All parties will ensure protection of subject personal data and will not include subject names or other identifiable data in any reports, publications, or other disclosures, except where required by laws.

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When study data are compiled for transfer to GSK CH and other authorized parties, subject names, addresses, and other identifiable data will be replaced by numerical codes based on a numbering system provided by GSK CH in order to de-identify study subjects.

The study site will maintain a confidential list of subjects who participated in the study, linking each subject's numerical code to his or her actual identity. In case of data transfer, GSK CH will maintain high standards of confidentiality and protection of subjects' personal data consistent with applicable privacy laws.

The informed consent documents must be in compliance with ICH GCP, local regulatory requirements, and legal requirements, including applicable privacy laws.

The informed consent documents used during the informed consent process must be reviewed and approved by the sponsor, approved by the IRB/EC before use, and available for inspection.

The investigator must ensure that each study subject, is fully informed about the nature and objectives of the study and possible risks associated with participation.

The investigator, or a person designated by the investigator, will obtain written informed consent from each subject before any study-specific activity is performed. The investigator will retain the original of each subject's signed informed consent document.

11.3.4 Subject Recruitment

Advertisements approved by IRBs and investigator databases may be used as recruitment procedures. Use of IRB approved, generic, pre-screening questionnaire to assess basic subject characteristics to determine general eligibility for this study is allowed. This generic questionnaire may be used by sites as a phone script and/or to review internal databases to identify subjects.

GSK CH will have an opportunity to review and approve the content of any study recruitment materials directed to potential study subjects before such materials are used.

11.3.5 Reporting of Safety Issues and Serious Breaches of the Protocol or ICH GCP

Within a GSK CH a serious breach is defined as a breach likely to affect to a significant degree the safety and rights of a subject or the reliability and robustness of the data generated in GSK CH- sponsored human subject research studies.


In the event of any prohibition or restriction imposed (i.e., clinical hold) by an applicable competent authority in any area of the world, or if the investigator is aware of any new information that might influence the evaluation of the benefits and risks of the investigational product, GSK CH should be informed immediately.

In addition, the investigator will inform GSK CH immediately of any urgent safety measures taken by the investigator to protect the study subjects against any immediate hazard, and of any serious breaches of this protocol or of ICH GCP that the investigator becomes aware of.

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11.4 Posting of Information on Publicly Available Clinical Trial Registers

Study information from this protocol will be posted on publicly available clinical trial registers before enrolment of subjects begins in accordance with applicable GSK processes.

11.5 Provision of Study Results to Investigators

Where required by applicable regulatory requirements, an investigator signatory will be identified for the approval of the clinical study report. The investigator will be provided reasonable access to statistical tables, figures, and relevant reports and will have the opportunity to review the complete study results at a GSK site or other mutually-agreeable location.

GSK will also provide the investigator with the full summary of the study results. The investigator is encouraged to share the summary results with the study subjects, as appropriate.

The procedures and timing for public disclosure of the results summary and for development of a manuscript for publication will be in accordance with GSK Policy.

A manuscript will be progressed for publication in the scientific literature if the results provide important scientific or medical knowledge.

11.6 Records Retention

Following closure of the study, the investigator must maintain all site study records (except for those required by local regulations to be maintained elsewhere), in a safe and secure location.

The records (study/ site master file) must be maintained to allow easy and timely retrieval, when needed (e.g., for a GSK audit or regulatory inspection) and must be available for review in conjunction with assessment of the facility, supporting systems, and relevant site staff.

Where permitted by local laws/regulations or institutional policy, some or all of these records can be maintained in a format other than hard copy (e.g., microfiche, scanned, electronic); however, caution needs to be exercised before such action is taken.

The investigator must ensure that all reproductions are legible and are a true and accurate copy of the original and meet accessibility and retrieval standards, including re-generating a hard copy, if required. Furthermore, the investigator must ensure there is an acceptable back-up of these reproductions and that an acceptable quality control process exists for making these reproductions.

The investigator must assure that the subject's anonymity will be maintained. On CRFs or other documents submitted to GSK CH, subjects should not be identified by their names or initials, but by an identification code. The investigator should keep a separate log of subjects' codes, names and addresses. Documents not for submission to GSK CH, e.g. subjects' written consent forms, should be maintained by the investigator in strict confidence.

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Records and documents, including signed ICF, pertaining to the conduct of this study must be retained by the investigator for 25 years from the issue of the final Clinical Study Report (CSR)/ equivalent summary unless local regulations or institutional policies require a longer retention period. The minimum retention time will meet the strictest standard applicable to that site for the study, as dictated by any institutional requirements or local laws or regulations, GSK standards/procedures, and/or institutional requirements.

No study document should be destroyed without a prior written agreement between GSK CH and the investigator. The investigator must notify GSK of any changes in the archival arrangements, including, but not limited to, archival at an off-site facility or transfer of ownership of the records in the event the investigator is no longer associated with the site.

11.7 Conditions for Terminating the Study

Premature termination of this study may occur because of a regulatory authority decision, change in opinion of the IRB/EC, or investigational product safety problems, or at the discretion of GSK CH. In addition, GSK CH retains the right to discontinue development of denture adhesives at any time.

If a study is prematurely terminated, GSK CH will promptly notify the investigator. After notification, the investigator must promptly contact all participating subjects and should assure appropriate therapy/ follow-up for the subjects. As directed by GSK CH, all study materials must be collected and all CRFs completed to the greatest extent possible. Where required by the applicable regulatory requirements, GSK CH should inform the regulatory authority(ies) and the investigator should promptly inform the IRB and provide the IRB/EC a detailed written explanation of the termination or suspension.

If the IRB/EC terminates or suspends its approval/favourable opinion of a trial, the investigator should promptly notify the GSK CH and provide GSK CH with a detailed written explanation of the termination or suspension.

Upon completion or premature discontinuation of the study, the GSK CH monitor will conduct site closure activities with the investigator or site staff, as appropriate, in accordance with applicable regulations including GCP, and GSK CH Standard Operating Procedures.

11.8 Definition of Study End/ End of Study

The end of the study will be the date of the Last Subject Last Visit (LSLV). For this study the LSLV date will be the primary completion date (PCD).

12 REFERENCES


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13 APPENDICES

13.1 ABBREVIATIONS

The following is a list of abbreviations that may be used in the protocol.


Table 13-1 Abbreviation

Abbreviation	Term
°C	Degree Centigrade
°F	Degree Fahrenheit
AE	Adverse Event
ANOVA	Analysis of Variance
CI	Confidence Interval
CRF	Case Report Form
CSA	Clinical Study Agreement
CTA	Clinical Trial Application
eCRF	Electronic Case Report Form
EudraCT	European Clinical Trials Database
FDA	Food and Drug Administration (United States)
FDAAA	Food and Drug Administration Amendments Act (United States)
g	Gram
GCP	Good Clinical Practice
GSK	GlaxoSmithKline
GSK CH	GlaxoSmithKline Consumer Healthcare
ICH	International Conference on Harmonisation
IRB	Institutional Review Board
LSLV	Last Subject Last Visit
MedDRA	Medical Dictionary for Regulatory Activities
N/A	Not Applicable
OST	Oral Soft Tissue
PI	Principal Investigator
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
SS	Safety Statement
US	United States

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13.2 Subject Completed Questionnaire

The following questions are about the peanut chewing you have just undertaken. Thinking about **only the peanuts you have just chewed** please circle one answer for each question.

1) Were you aware of peanuts under your denture? (Please circle your answer)

Yes

No

Only answer questions 2-4 if you circled "Yes" for question 1 above.

2) On a scale of 1 to 10 how would you rate the **amount** of peanut particles that went under your denture? (Please circle your answer)


1 2 3 4 5 6 7 8 9 10
None Numerous

3) On a scale of 1 to 10 how would you rate the **irritation** of peanuts under your denture? (Please circle your answer)

1 2 3 4 5 6 7 8 9 10
Not at all Irritating Extremely Irritating

4) On a scale of 1 to 10 how **bothered** were you by the peanuts that went under your denture? (Please circle your answer)

1 2 3 4 5 6 7 8 9 10
Not at all Bothered Extremely Bothered

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13.3 Product Application Instructions

Randomisation Code []

For application per conventional pattern....




1. Extrude and dispose of first 1-2 inches of product from each tube to ensure product consistency.
2. Pre-load 2 syringes with $1.00 \pm 0.05\text{g}$ and $0.60 \pm 0.05\text{g}$ of denture adhesive for the maxillary and mandibular denture respectively. Syringes should be labelled. Store the syringes capped and do not store for longer than 4 hours. Syringes will be labelled with subject or randomisation number and identifying text for maxillary or mandibular application.
3. Clean and dry dentures.
4. Apply product via the pre-weighed syringe in short strips as shown in the diagram, not too close to the denture edges (3 strips should be applied to the upper denture and 2 on the lower denture). All of the adhesive in the pre-weighed syringe should be used.
5. Have the subject rinse their mouth with water and expectorate before inserting the dentures.
6. Have the subject press dentures into place firmly, and bite down for a few seconds to secure hold.

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Randomisation Code []

For application per continuous strips pattern....




1. Extrude and dispose of first 1-2 inches of product from each tube to ensure product consistency.
2. Pre-load 2 syringes with $1.00 \pm 0.05\text{g}$ and $0.60 \pm 0.05\text{g}$ of denture adhesive for the maxillary and mandibular denture respectively. Store the syringes capped and do not store for longer than 4 hours. Syringes will be labelled with the subject or randomisation number and identifying text for maxillary or mandibular application.
3. Clean and dry dentures.
4. Apply product via a pre-weighed syringe in long, continuous strips as shown in the diagram, not too close to the denture edges (3 strips should be applied to the upper denture and 1 on the lower denture). All of the adhesive in the pre-weighed syringe should be used.
5. Have the subject rinse their mouth with water and expectorate before inserting the dentures.
6. Have the subject press dentures into place firmly, and bite down for a few seconds to secure hold.

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Randomisation Code []

For application of no adhesive....

1. Clean and dry dentures.
2. Have the subject rinse their mouth with water and expectorate before inserting the dentures.
3. Have the subject press dentures into place firmly, and bite down for a few seconds to secure hold.

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the PRO data is entered into the DMS by GSK CH, the PROs will be anonymised as agreed and documented prior to study initiation. PROs that are source will be retained by the investigator and certified copies will be sent to GSK CH.

In order to protect the privacy of subjects, no Personally Identifiable Information (PII) (including the subject's name or initials or birth date) is to be recorded on all PRO's that will be forwarded to GSK CH.

All PRO source data should be reviewed by the study staff/study monitor (as appropriate) to ensure that any potential AEs reported on these documents are represented in the DMS.

9.5 External Data

External Data are subject data obtained externally to the CRF. These data are generated from laboratory instruments, computers or other sources and then transcribed into a file and format agreed upon by GSK CH to identify the subject and time point referenced in the CRF and/or protocol.

An agreed upon quality control process is performed against the transcribed data to the source to ensure the accuracy of the transcription. The transcribed data is transmitted in an agreed upon format to GSK CH.

Reconciliation will be performed between the transcribed data and the clinical database to ensure subject and time point referenced in the Clinical Database match before Clinical Database Freeze (locking of the database) can occur.

10 STATISTICAL CONSIDERATIONS AND DATA ANALYSES

10.1 Sample Size Determination



Since this is an exploratory methodology development study, no formal sample size calculation was conducted. CCI

Therefore, approximately 48 (maximum 50) healthy subjects with both maxillary and mandibular full dentures will be enrolled in this study. Subject recruitment will be controlled to ensure 50±10% of the subjects will be in each of the low and high Kapur-Olshan groups [the low Kapur-Olshan group is defined as a composite Kapur-Olshan score of 6-14 (clinically fair and good dentures) and the high Kapur-Olshan score as 15-18 (clinically very good dentures)].

10.2 Statistical Methods and Analytical Plan

Additional details of the proposed statistical analysis will be documented in the statistical analysis plan (SAP), which will be written following finalisation of the protocol and prior to study unblinding / analysis (as appropriate).

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