Clinical Protocol

206233

CONFIDENTIAL

SUMMARY INFORMATION

Title:	A Proof of Principle Bite Force Study Using Two New Test Adhesives and a Currently Marketed Denture Adhesive
Protocol Number:	206233
Sponsor:	GlaxoSmithKline Consumer Healthcare (GSKCH) 184 Liberty Corner Road, Warren NJ, 07059, United States Tel: PPD
Product Name:	Super Poligrip® and two PVA-based experimental denture adhesives
Development Phase:	N/A

Expert Advice Outside of Normal Working Hours:	Tel: PPD

Key Protocol Authors:	
PRIMARY CONTACT **Clinical Study Manager:**	PPD PPD, BS GSKCH 184 Liberty Corner Road, Warren NJ, 07059, United States Tel: PPD
Clinical Research:	PPD, PhD, BDS, MFDSRCS, MFGDP, FHEA GSKCH St. George's Avenue, Weybridge, Surrey, KT13 0DE, United Kingdom (UK)
Biostatistician:	PPD, PhD inVentiv Health Clinical PPD

	PPD India
Clinical Supplies:	PPD GSKCH St. George's Avenue, Weybridge, Surrey, KT13 0DE, United Kingdom (UK)

Principal Investigator:	Thomas DiLauro, DMD
Study Site Name & Address:	TKL Research, 1255 Broad Street, Bloomfield, NJ 07003
Study Site Telephone Number:	PPD

Product Name:	Super Poligrip® Free & two PVA-based test denture adhesive formulations
IND/EUDRACT No:	N/A
Phase of Study:	N/A

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:	Dr. Thomas DiLauro
Investigator Qualifications:	DMD
Investigator Signature:	PPD
Date of Signature/ Agreement:	PPD DD/MMM/YYYY

Table of Content

PROCESS FOR AMENDING THE PROTOCOL

Protocol modifications to ongoing studies which could potentially adversely affect the safety of subjects or which alter the scope of the investigation, the scientific quality of the study, the experimental design, dosages, duration of therapy, assessment variables, the number of subjects treated, or subject selection criteria are considered major/substantial amendments and must be made only after appropriate consultation between an appropriate representative of GSKCH and the investigator.

Details of amendments to the protocols should be recorded on the following page. Protocol modifications must be prepared by a representative of GSKCH. All changes must be justified in the Reason for Amendment section of the following Protocol Amendment Page. Approval of amendments will be made by the original protocol signatories or their appropriate designees.

All major/substantial protocol modifications must be reviewed and approved by the appropriate IRB in accordance with local requirements, before the revised edition can be implemented.

All non-substantial/ minor/ administrative amendments should be submitted to the IRB as per country specific requirements. In some countries pre-approval of a minor amendment is not required and will just be held on file by the sponsor and investigator.

PROTOCOL AMENDMENT PAGE

Details of all amendments should be recorded in the table below. Affected sections should be listed in the table; the actual amendment/ change should be made in the relevant section of the main protocol.
To highlight the change, the following features will be used:
To **add** text: Use of **CAPITAL LETTERS, BOLD AND UNDERLINE**
To **delete** text: Use of Strikethrough e.g. ~~strikethrough~~

Amendment No. & New Protocol Version No.	Type of Amendment	Reason for Amendment	Other Documents Requiring Amendment	Section(s) Amended	PI Amendment Agreement Signature & Date
Amendment No.: 1	Non-Substantial/Minor ☒	This is Protocol amendment 1 (Protocol version 5.0) as previous amendments (2.0, 3.0 and 4.0) were made prior to Ethics submission. Change of Clinical Study Manager details. To correct inconsistencies from which point AEs and incidents should be collected.	Informed Consent ☐ Yes ☒ No Safety Statement ☐ Yes ☒ No CRF ☐ Yes ☒ No	Summary Information. Schedule of events. Study Design (Synopsis & Section 3.1). 6.2.3 Bite Force Measures during Treatment Visits. 7.2 Recording Adverse Events and Serious Adverse Events.	Signature: PPD
Protocol Version No.: 5.0	Substantial/ Major ☐				Date: PPD

Amendment No.:	Non-Substantial/Minor ☐		Informed Consent ☐ Yes ☐ No Safety Statement ☐ Yes ☐ No CRF ☐ Yes ☐ No		Signature:
Protocol Version No.:	Substantial/ Major ☐				Date:

SCHEDULE OF EVENTS

Procedure/ Assessment	Screening		Treatment 1		Treatment 2		Treatment 3		Treatment 4
	Visit 1	Between 1-14 days of screening	Visit 2	Between 1-14 days	Visit 3	Between 1-14 days	Visit 4	Between 1-14 days	Visit 5
Informed Consent	X								
Subject Demographics	X								
Medical History	X								
Dental History	X								
Current/Concomitant Medications	X		X		X		X		X
Kapur Index Assessment for well made & fitting dentures (retention, stability, fit & clinical acceptability)	X								
Inclusion/Exclusion	X		X						
Oral Soft Tissue (OST) assessment – Edentulous	X		X[1]		X[1]		X[1]		X[1]
Denture Bearing Tissue Score	X								
Denture Cleansing	X		X		X		X		X
Mandibular Denture Stabilization[2]	X		X		X		X		X
Three Incisal Bite Force readings with no adhesive	X[3]		X[4]		X[4]		X[4]		X[4]
Incisal Bite Force with no adhesive	X[5]		X[6]		X[6]		X[6]		X[6]
Subject Eligibility/ adherence	X		X						
Adverse Events/Incident Reporting[7]	X		X		X		X		X
Continued Eligibility			X		X		X		X
Randomization			X						
Product Application by site staff to maxillary denture[8]			X[8]		X[8]		X[8]		X[8]
Incisal Bite Force			X[9]		X[9]		X[9]		X[9]

Measurements[9]								
Subject administered questions around product ooze at 0.5 hour[10]			X		X		X	X
Subjects administered questions around flavor, texture and extrusion of the adhesive from the tube[11]			X		X		X	X
Removal of denture from the mouth by subject			X		X		X	X
Completion of denture removal questionnaire[12]			X		X		X	X
Remove product from denture before dismissing subject			X		X		X	X
Post treatment OST			X		X		X	X
Adverse Events/Incident Reporting[7]	X		X		X		X	X
Study Conclusion								X

[1] OST on Test Day is for pre-treatment baseline
[2] Mandibular Denture stabilization with adhesive (if necessary; at the discretion of the Investigator)
[3] Bite force readings at Screening Visit are "training"
[4] Bite Force readings on Test Day are "practice"
[5] Incisal Bite Force at Screening visit is 'Qualifying'
[6] Incisal Bite Force on Test Day is pre-treatment "baseline"
[7] Adverse Events and Incidents will be assessed from the OST examination at screening ~~and pre and post bite force recordings on the Test Days~~
[8] Dentures of subjects randomized to a denture adhesive treatment shall be weighed before & after adhesive application to ensure correct dose applied
[9] Incisal Bite Force Measurements at t= 0.5, 1, 3, 6, 9 and 12 hours post adhesive application
[10] Subjects will complete the Product Ooze Questionnaire immediately following the 0.5 hr bite incisal bite force measure
[11] Subjects will complete the Sensory including Product Extrusion Questionnaire immediately following the last (12 hr) incisal bite force measure
[12] Subjects will complete the Denture Removal Questionnaire immediately following upper denture removal by the subject

PROTOCOL SYNOPSIS FOR STUDY 206233

Brief Summary

The objective of this 4-treatment, 4-period, randomized, crossover, proof of principle bite force study is to compare bite force measurements over a 12 hour period across two newly formulated (test) cream denture adhesives based on a new polymer technology, with a currently marketed cream denture adhesive (positive control), and a negative/no treatment control. The test products comprise 2 new denture adhesive formulations that are based on a new water insoluble and heat-resistant polyvinyl acetate (PVA) polymer based formulation with a new solvent system to try to achieve better complete denture hold and food sealing. Super Poligrip® Free, a commercially available denture adhesive product marketed by GSKCH in the United States (US), will be used as the positive control. A short questionnaire regarding the flavor and texture characteristics of each denture adhesive after a single use will also be administered to give an indication of subject satisfaction of these attributes.

In this study, a bite force transducer system will be used to measure incisal bite force until dislodgement of maxillary complete dentures. Subjects in this study will have dentures judged to be clinically acceptable/moderately well fitting using the Kapur criteria that was modified by Olshan *et al.* in 1992. Dentures will also be judged to be well made using the design and construction criteria used previously [GSK studies CCI]. Bite force measurements will be taken over a 12-hour time period to compare treatments.

This study is planned to be conducted at TKL Research based in Bloomfield, New Jersey, USA, and subjects will be recruited via the TKL database.

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Objectives and Endpoints

Objectives	Endpoints
Primary	
To compare incisal bite force for test adhesive 1 versus no adhesive after 12 hours.	Area Over Baseline (AOB) at 12 hours.
To compare incisal bite force for test adhesive 2 versus no adhesive after 12 hours.	AOB at 12 hours.
Secondary	
To compare incisal bite force for test adhesive 1 versus Super Poligrip® Free after 12 hours.	AOB at 12 hours.
To compare incisal bite force for test adhesive 2 versus Super Poligrip® Free after 12 hours.	AOB at 12 hours.
To compare incisal bite force between test adhesives 1 & 2 after 12 hours.	AOB at 12 hours.
Other	
To compare incisal bite force for test adhesive 1 versus no adhesive over 9 hours.	AOB at 0.5, 1, 3, 6 and 9 hours.
To compare incisal bite force for test adhesive 2 versus no adhesive over 9 hours.	AOB at 0.5, 1, 3, 6 and 9 hours.
To compare incisal bite force for test adhesive 1 versus Super Poligrip® Free over 9 hours.	AOB at 0.5, 1, 3, 6 and 9 hours.
To compare incisal bite force for test adhesive 2 versus Super Poligrip® Free over 9 hours.	AOB at 0.5, 1, 3, 6 and 9 hours
To assess subjects' preference with regards to denture adhesive ooze, flavor/ after-taste, texture and assess ease of removal	Scores from subject-completed questionnaires on product ooze, at 0.5 hours, and flavour/ after-taste, texture and ease of removal after 12 hours' use
To assess the ease of extrusion of the product from the tube by the subjects post bite force phase	Scores from subject-completed questionnaire on product extrusion after 12 hours' use

Study Design

Overall Design

This single centre, randomized, crossover, proof-of-principle study will be a randomized four period, four treatment, examiner blind [to the examiner performing the bite force & oral soft tissue (OST) examinations] design in subjects with well made and moderately well-fitting maxillary complete dentures. Informed consent will be obtained from participants before the implementation of any study procedure.

At the Screening Visit, subjects will be screened for eligibility and ability to perform the bite force manoeuvre according to stated inclusion/exclusion criteria. On the test day visit, subjects will report to the study site without adhesive placed in their dentures. Dentures will be removed and cleaned. An OST examination will be performed before the lower denture (if applicable) is secured using Super Poligrip® Flavour Free denture adhesive, whilst the upper denture is removed, and the pre-treatment baseline incisal bite force measurements will be obtained (both practice bites and qualifying test bite). To maintain blinding, subjects must not disclose to the examiner if they are wearing adhesive or no adhesive. Subjects meeting all the inclusion criteria with no exclusions will then be randomized at Visit 2.

On each test day (Visits 2-5) subjects will undergo an OST examination and have their dentures cleaned. Denture adhesive treatment (or no treatment as per the randomization schedule) will then be applied by a member of study staff (ideally the same member of staff throughout the study) as per the application instructions, and the dentures worn by the subject. Incisal bite force measurements will be made at 0.5, 1, 3, 6, 9 and 12 hours after the dentures are placed in the mouth. After 0.5 hours assessment the subjects will be asked to complete questions about product ooze (Appendix II). The questions will be completed by the subjects themselves and these responses will then be given to study site staff to transfer to the eCRF.

Immediately following the last (12 hour) incisal bite force measurement, subjects will be asked to complete a short questionnaire relating to the after-taste and texture of the denture adhesive when randomized to one of the denture adhesive treatment periods (Appendix III). This will be completed by the subject themselves in a quiet environment without external influence.

Immediately following subsequent upper denture removal by the subjects themselves, subjects will be asked to answer another short questionnaire (which will be administered by the site staff; Appendix IV) pertaining to ease of removal of the

denture when undertaking the treatment phases of the study, but not the negative no treatment control arm. The subjects will remove their dentures by themselves under supervision by site staff. Following denture removal, and completion of the associated questionnaire, site staff will clean the denture before returning to the patient at the end of the study.

These assessments will be followed by the final post-treatment OST examination.

These procedures will be repeated in a crossover manner. There will be at least 24 hours (up to 14 days) between treatment visits to allow recovery from the bite force procedures.

Visit 1 - Screening Visit

The following assessments will be conducted:

- Written informed consent.
- Demographics, medical history, current/concomitant medications, and dental history.
- Criteria for well-made dentures
- Inclusion/exclusion criteria
- Oral soft tissue examination including edentulous maxillary arch
- Denture bearing tissue score
- Kapur Index assessment
- Denture cleansing
- Mandibular denture stabilization (with adhesive, if deemed to be necessary to ensure accurate bite force measures; at the discretion of the Investigator)
- Three incisal bite force readings with no adhesive on upper denture (for training)
- Incisal bite force with no adhesive on the upper denture (qualifying)
- Inclusion/exclusion criteria (following initial bite force measures)
- Subject eligibility
- Adverse events and incident reporting (assessed from the **OST EXAMINATION AT SCREENING** ~~start of the first bite force measurement~~)

Visits 2, 3, 4 & 5

The following assessments will be conducted:

- Review of current/concomitant medications, adverse events and incidents
- Oral soft tissue examination including edentulous maxillary arch
- Denture cleansing
- Mandibular denture stabilization (with adhesive, if deemed to be necessary to ensure accurate bite force measures; at the discretion of the Investigator)

- Three incisal bite force readings with no adhesive on the upper denture (for practice)
- Incisal bite force with no adhesive on the upper denture (pre-treatment "baseline")
- Subject eligibility
- Adverse events and incident reporting (assessed pre bite force measurement)
- Continued eligibility
- Randomisation (Test/Treatment day 1 only)
- Weigh maxillary denture prior to adhesive placement.
- Product application by site staff to maxillary denture (or no adhesive for the no adhesive negative control)
- Weigh maxillary denture immediately following adhesive placement (record weight difference i.e. weight of adhesive used to ensure correct dose applied)
- Dentures of subjects randomized to a denture adhesive shall be weighed before & after adhesive application
- Upper denture insertion by subject
- Incisal bite force measurements (at 0.5 hours prior to product ooze questionnaire (Appendix II), followed by 1, 3, 6, 9 & 12 hours post adhesive application)
- Subject evaluation questionnaire (product ooze) 0.5 hours post adhesive application (Appendix II)
- Subject sensory questionnaire (flavour, texture and extrusion of the adhesive from the tube; Appendix III) immediately following the last (12 hr) bite force measure whilst upper denture still retained in the mouth
- Removal of denture from the mouth by the subject
- Denture adhesive retention questionnaire completed by Examiner/ site staff
- Removal of excess adhesive from the mouth by the subject facilitated by site study staff as and where necessary
- Subject denture removal questionnaire (Appendix IV) immediately following 12 hour post adhesive application bite force measure, completion of subject sensory questionnaire and subsequent removal of the upper denture
- Study Staff to check denture removal questionnaire completion to ensure that any AEs which have been noted in the questionnaire free text is reviewed and captured in the eCRF before the subjects leave
- Post-treatment oral soft tissue examination by a blinded examiner
- Dentures cleaned and returned to subject
- Adverse events and incident reporting (assessed post bite force measurement)

There will be at least 24 hours (up to 14 days) between subsequent treatment days to allow recovery from the bite force procedures.

Type and Planned Number of Subjects

Approximately 25 subjects will be screened to randomize approximately 21 subjects to ensure that approximately 18 evaluable subjects complete the study.

Diagnosis and Main Criteria for Inclusion

Healthy male and female subjects, aged between 18 to 85 years of age, selected from the TKL Research volunteer database. Subjects must have a completely edentulous maxilla restored with well to moderately well fitting and well made conventional full maxillary denture and a maxillary incisal bite force (without adhesive) that is less than or equal to 9 pounds (lbs), at the Screening Visit.

Product Information

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

	Test Product 1	Test Product 2	Reference Product	Negative Control
Product Name	Test adhesive 1 with a thin nozzle	Test adhesive 2 with a thin nozzle	Super Poligrip® Free Adhesive Cream (USA marketplace)	No adhesive
Product Formulation Code (MFC)	CCI	CCI	CCI	N/A
Dose	Continuous strips applied to upper denture as per the application instructions	Continuous strips applied to upper denture as per the application instructions	3 dabs for upper denture as per the product label application instructions	N/A
Route of Administration	Oral topical	Oral topical	Oral topical	N/A
Dosing Instructions	applied to clean dry denture fit surface in a pattern consistent with the application instructions	applied to clean dry denture fit surface in a pattern consistent with the application instructions	applied to clean dry denture fit surface in a pattern consistent with the product label application instructions	N/A

Statistical Methods

The Area Over Baseline (AOB) over 12 hours for the incisal bite force (lbs) (denoted by AOB_{0-12}) is the primary efficacy variable. To calculate this variable first the Area Under the Curve (AUC) is calculated from 0 to 12 hours (AUC_{0-12}) using the trapezoid method. AOB_{0-12} will be calculated as $(AUC_{0-12})/12$ minus baseline bite force (lbs). An Analysis of Covariance (ANCOVA) model will be used to analyse AOB_{0-12}, with treatment and period as fixed effects; the covariates in this model are the subject level baseline and period level baseline minus subject level baseline. Subject will be included as a random effect.

If statistical significance is not obtained for at least one test adhesive vs no adhesive then the study validity will be evaluated by comparing Super Poligrip® Free vs no adhesive.

AOB for 0.5, 1, 3, 6 and 9 hours will be defined and analysed in a similar manner as AOB_{0-12}.

Subject questionnaire and denture adhesive weight data will be summarized using summary statistics only and no formal statistical analyses will be performed.

1. INTRODUCTION

Denture adhesives or fixatives have been used by edentulous patients to improve the retention and stability of dentures for many years. The primary benefit of using a denture adhesive is to enhance treatment outcome by increasing retention of the prosthesis and by reducing food entrapment (Zarb & Fenton 2013).

There are a number of recognized methods which have been used to demonstrate the effectiveness of a denture adhesive. These include the Kapur Index (Kapur et al. 1967) and bite force until denture dislodgement (Howell et al. 1948) to measure denture retention and stability, denture dislodgement (Tarbet et al. 1980) to measure denture movement in function, and masticatory performance (Kapur et al. 1967) an indicator of chewing efficiency. This study investigates bite force as a measurement of retention of the maxillary denture.

The objective of this 4-treatment, 4-period, randomized, crossover, proof of principle bite force study is to compare bite force measurements over a 12 hour period across two newly formulated (test) cream denture adhesives based on a new polymer technology, with a currently marketed cream denture adhesive (positive control), and a negative/no treatment control. The test products comprise 2 new denture adhesive formulations that are based on a new water insoluble and heat-resistant polyvinyl acetate (PVA) polymer based formulation with a new solvent system to try to achieve better complete denture hold and food sealing. Super Poligrip® Free, a commercially available denture adhesive product marketed by GSKCH in the United States (US), will be used as the positive control. A short questionnaire regarding the flavor and texture characteristics of each denture adhesive after a single use will also be administered to give an indication of subject satisfaction of these attributes.

In this study, a bite force transducer system will be used to measure incisal bite force until denture dislodgement of maxillary complete dentures. Subjects in this study will have dentures judged to be clinically and acceptable/moderately well fitting using the Kapur criteria that was modified by Olshan et al. in 1992. Dentures will also be judged to be well made using the design and construction criteria used previously (GSK studies CCI [redacted]). Bite force measurements will be taken over a 12-hour time period to compare the strength of the two test adhesives over time against the positive control adhesive over time with the aim of demonstrating a statistically significant difference, and to compare the three denture

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adhesives to bite force readings (Area over the Baseline) taken without the use of adhesive.

Studies using bite force as a clinical model have routinely utilized a sample size of 35-50 subjects with clinically poor (Kapur et al. 1967) maxillary dentures. In this population, the bite force clinical model has been used successfully to demonstrate that cream denture adhesives improve denture hold for 12 hours and to also demonstrate differences in strength among various adhesive formulations. The dental literature also contains a number of studies that indicate benefits for other brands or formulations of denture adhesive in well fitting dentures (Chew et al. 1984, 1985, Grasso et al. 2004).

Previous GSK studies (CCI [redacted]) with sample sizes of 22-45 subjects have demonstrated that statistically significant increases in bite force can be achieved with well-fitting and well-made dentures one hour after the application of denture adhesives and denture powders. GSK only promotes the use of denture adhesives in well-fitting dentures. Hence in this study, subjects with moderately well-fitting dentures will be the test population.

2. OBJECTIVES AND ENDPOINTS

Objectives	Endpoints
Primary	
To compare incisal bite force for test adhesive 1 versus no adhesive after 12 hours.	AOB at 12 hours.
To compare incisal bite force for test adhesive 2 versus no adhesive after 12 hours.	AOB at 12 hours.
Secondary	
To compare incisal bite force for test adhesive 1 versus Super Poligrip® Free after 12 hours.	AOB at 12 hours.
To compare incisal bite force for test adhesive 2 versus Super Poligrip® Free after 12 hours.	AOB at 12 hours.
To compare incisal bite force between test adhesives 1 & 2 after 12 hours.	AOB at 12 hours.
Other	
To compare incisal bite force for test adhesive 1 versus no adhesive over 9 hours.	AOB at 0.5, 1, 3, 6 and 9 hours.
To compare incisal bite force for test adhesive 2 versus no adhesive over 9 hours.	AOB at 0.5, 1, 3, 6 and 9 hours.
To compare incisal bite force for test adhesive 1 versus Super Poligrip® Free over 9 hours.	AOB at 0.5, 1, 3, 6 and 9 hours.
To compare incisal bite force for test adhesive 2 versus Super Poligrip® Free over 9 hours.	AOB at 0.5, 1, 3, 6 and 9 hours
To assess subjects' preference with regards to denture adhesive ooze, flavor/ after-taste, texture and assess ease of removal	Scores from subject-completed questionnaires on product ooze, at 0.5 hours, and flavour/ after-taste, texture and ease of removal after 12 hours' use
To assess the ease of extrusion of the product from the tube by the subjects post bite force phase	Scores from subject-completed questionnaire on product extrusion after 12 hours' use

3. STUDY PLAN

3.1. Study Design

Overall Design

This single centre, randomized, crossover, proof-of-principle study will be a randomized four treatment, examiner blind [to the examiner performing the bite force & oral soft tissue (OST) examinations] design in subjects with well made and moderately well-fitting maxillary complete dentures. Informed consent will be obtained from participants before the implementation of any study procedure.

At the Screening Visit, subjects will be screened for eligibility and ability to perform the bite force manoeuvre according to stated inclusion/exclusion criteria. On the test day visit, subjects will report to the study site without adhesive placed in their dentures. Dentures will be removed and cleaned. An OST examination will be performed before the lower denture (if applicable) is secured using Super Poligrip® Flavour Free denture adhesive, whilst the upper denture is removed, and the pre-treatment baseline incisal bite force measurements will be obtained (both practice bites and qualifying test bite). To maintain blinding, subjects must not disclose to the examiner if they are wearing adhesive or no adhesive. Subjects meeting all the inclusion criteria with no exclusions will then be randomized at Visit 2.

On each test day (Visits 2-5) subjects will undergo an OST examination and have their dentures cleaned. Denture adhesive treatment (or no treatment as per the randomization schedule) will then be applied by a member of study staff (ideally the same member of staff throughout the study) as per the application instructions, and the dentures worn by the subject. Incisal bite force measurements will be made at 0.5, 1, 3, 6, 9 and 12 hours after the dentures are placed in the mouth. After 0.5 hours assessment the subjects will be asked to complete questions about product ooze (Appendix II). The questions will be completed by the subjects themselves and these responses will then be given to study site staff to transfer to the eCRF.

Immediately following the last (12 hour) incisal bite force measurement, subjects will be asked to complete a short questionnaire relating to the after-taste and texture of the denture adhesive (Appendix III). This will be completed by the subject themselves in a quiet environment without external influence.

Immediately following subsequent upper denture removal by the subjects themselves, subjects will be asked to answer another short questionnaire (which will be

administered by the site staff; Appendix IV) pertaining to ease of removal of the denture when undertaking the treatment phases of the study, but not the negative no treatment control arm. The subjects will remove their dentures by themselves under supervision by site staff. Following denture removal, and completion of the associated questionnaire, site staff will clean the denture before returning to the patient at the end of the study.

These assessments will be followed by the final post-treatment OST examination.

These procedures will be repeated in a crossover manner. There will be at least 24 hours (up to 14 days) between treatment visits to allow recovery from the bite force procedures.

Visit 1 - Screening Visit

The following assessments will be conducted in the order written:

- Written informed consent.
- Demographics, medical history, current/concomitant medications, and dental history.
- Criteria for well made dentures
- Inclusion/exclusion criteria
- Oral soft tissue examination including edentulous maxillary arch
- Denture bearing tissue score
- Kapur Index assessment
- Denture cleansing
- Mandibular denture stabilization (with adhesive, if deemed to be necessary to ensure accurate bite force measures; at the discretion of the Investigator)
- Three incisal bite force readings with no adhesive on upper denture (for training)
- Incisal bite force with no adhesive on the upper denture (qualifying)
- Inclusion/exclusion criteria (following initial bite force measures)
- Subject eligibility
- Adverse events and incident reporting (assessed from the **OST EXAMINATION AT SCREENING** ~~start of the first bite force measurement~~)

Visits 2, 3, 4 & 5

The following assessments will be conducted:

- Review of current/concomitant medications, adverse events and incidents
- Oral soft tissue examination including edentulous maxillary arch
- Denture cleansing
- Mandibular denture stabilization (with adhesive, if deemed to be necessary to

ensure accurate bite force measures; at the discretion of the Investigator)

- Three incisal bite force readings with no adhesive on the upper denture (for practice)
- Incisal bite force with no adhesive on the upper denture (pre-treatment "baseline")
- Subject eligibility
- Adverse events and incident reporting (assessed pre bite force measurement)
- Continued eligibility
- Randomisation (Test/Treatment day 1 only)
- Weigh maxillary denture prior to adhesive placement
- Product application by site staff to maxillary denture (or no adhesive for the no adhesive negative control)
- Weigh maxillary denture immediately following adhesive placement (record weight difference i.e. weight of adhesive used to ensure correct dose applied)
- Dentures of subjects randomized to a denture adhesive shall be weighed before & after adhesive application
- Upper denture insertion by subject
- Incisal bite force measurements (at 0.5 hours prior to product ooze questionnaire (Appendix II), followed by 1, 3, 6, 9 & 12 hours post adhesive application)
- Subject evaluation questionnaire (product ooze) 0.5 hours post adhesive application (Appendix II)
- Subject sensory questionnaire (flavour, texture and extrusion of the adhesive from the tube; Appendix III) immediately following the last (12 hr) bite force measure whilst upper denture still retained in the mouth
- Removal of denture from the mouth by the subject
- Denture adhesive retention questionnaire completed by Examiner/ site staff
- Removal of excess adhesive from the mouth by the subject facilitated by site study staff as and where necessary
- Subject denture removal questionnaire (Appendix IV) immediately following 12 hour post adhesive application bite force measure, completion of subject sensory questionnaire and subsequent removal of the upper denture
- Study Staff to check denture removal questionnaire completion to ensure that any potential AEs which may have been noted in the questionnaire free text is reviewed and captured in the eCRF before the subject leaves the site
- Post-treatment OST by a blinded examiner
- Dentures cleaned and returned to subject
- Adverse events and incident reporting (assessed post bite force measurement)

There will be at least 24 hours (up to 14 days) between subsequent treatment days to

allow recovery from the bite force procedures.

3.2. Subject Restrictions

Lifestyle/ Dietary

During the entire study (screening to LSLV):

- Subjects will be instructed to report to the clinic on the treatment visit days without the presence of denture adhesive in either their maxillary or mandibular denture.
- Subjects will be required to remain on site for the duration of the treatment visit day. Standardized meals will be provided.
- On the test days, subjects' intake of hot & cold liquids will be restricted.
- Smoking, including e-cigarettes and the use of chewing tobacco or other tobacco products are prohibited for the duration of screening and on each test day.
- If subjects were using denture adhesives to stabilize their dentures, then they can continue using the denture adhesives during the washout periods between treatment visits only, but they cannot change it during the course of the study.
- Subjects should not consume any food or liquid an hour before the treatment visit. Subjects can consume small sips of water for medications.
- Subjects are not permitted to chew gum throughout the study.

Medications and Treatments

During the entire study (screening to LSLV):

- The details of current and concomitant medications will be collected and subjects will be allowed to participate if these medications are judged to be non-interfering by the investigator.
- Subjects will not be permitted to have any dental/denture work performed during the time that 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.

3.3. Type and Planned Number of Subjects

Approximately 25 subjects will be screened to randomize approximately 21 subjects to ensure that approximately 18 evaluable subjects complete the study.

3.4. Study Design and Dose Justification

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). A crossover design has been chosen because bite force measurements have high inter-subject variation; the crossover design will allow each subject to act as their own control.

Incisal bite force until denture dislodgement is a measure of maxillary denture retention and is a recognized objective test method that has been used to demonstrate the efficacy of denture adhesives.

A screening bite force will be taken to allow subjects to train in how to bite in a consistent manner for bite force technique and to allow the examiner to establish whether subjects understand and are able to conduct the necessary manoeuvres. Baseline bite force will be taken on each test day to allow the subjects to train and practice the bite force technique at each visit.

To minimize the possibility of carryover effects from study treatments or procedures, a washout period of at least 24 hours has been scheduled between each treatment visit.

The study will be blinded with respect to the dental examiner performing the bite force measures and OST examination in order to reduce the risk of bias. The subjects will not be blinded to the study treatments and will be instructed not to disclose their treatment to the examiner.

Super Poligrip® Free has been selected as the positive control adhesive in this study as it is a currently marketed and a representative denture adhesive of the denture adhesive market. The test adhesives in this study are experimental formulations – inclusion of these test adhesives will enable assessment of difference against a currently marketed, representative denture adhesive to assess whether these adhesives are suitable candidates to progress for further investigation.

The dosing regimen will be consistent with the product application instructions in the case of the marketed positive control, and consistent with product design and consumer habit for the experimental test adhesives. Denture adhesives are only promoted and recommended in well-fitting dentures, and therefore only well-fitting dentures are permitted for inclusion in this study.

A no adhesive negative control arm has been chosen to provide a continual reference point of no adhesive use over the 12 hour period. This should allow interpretation of the results of this study with previous work, and is representative of a significant number of denture wearers who currently do not use an adhesive. Use of the no

adhesive control will allow for variation in bite force technique over the test period, and enables Area over Baseline (AOB) comparison of the positive and negative controls over the 12 hour period.

4. SELECTION OF STUDY POPULATION AND WITHDRAWAL CRITERIA

Specific information regarding warnings, precautions, contraindications, adverse events, and other pertinent information on the GSK investigational product or other study treatment that may impact subject eligibility is provided in the product label.

Deviations from inclusion and exclusion criteria are not allowed because they can potentially jeopardize the scientific integrity of the study, regulatory acceptability or subject safety. Therefore, adherence to the criteria as specified in the protocol is essential.

4.1. Inclusion Criteria

A subject will be eligible for inclusion in this study only if all of the following criteria apply:

1. CONSENT
Demonstrates understanding of the study procedures, restrictions and willingness to participate as evidenced by voluntary written informed consent and has received a signed and dated copy of the informed consent form.

2. AGE
Aged between 18 to 85 years.

3. GENERAL HEALTH
Good general and mental health with, in the opinion of the investigator or medically qualified designee: a. No clinically significant and relevant abnormalities in medical history or upon oral examination. b. Absence of any condition that could affect the subject's safety or wellbeing or their ability to understand and follow study procedures and requirements.

4. DIAGNOSIS

a. Completely edentulous maxillary arch restored with a conventional full acrylic based upper complete denture.
b. Dentate, partial or full edentulous mandibular arch. Partial or full edentulous arch may be restored with a stable complete, partial or implant supported denture.
c. Maxillary dentures must be considered to be moderately well-fitting at the screening visit (Kapur Index, Olshan Modification: retention score ≥2, stability score ≥2).
d. Maxillary dentures and mandibular dentures, if present, must be considered to be well-made based on design and construction criteria specified in the protocol.
e. The qualifying maxillary incisal bite force readings (without adhesive) must be less than or equal to 9 pounds at the Screening Visit and subsequent visit pre-treatment baseline bites.
f. At least 2 of the 4 qualifying bite readings at the Screening Visit must be reproducible (±2lb). At subsequent visits the bite force readings must be within ±2lb for 1 of the 3 practice bites and the pre-treatment baseline bite.

5. COMPLIANCE
Understands and is willing, able and likely to comply with all study procedures and restrictions.

4.2. Exclusion Criteria

A subject will not be eligible for inclusion in this study if any of the following criteria apply:

1. PREGNANCY
A woman who is known to be pregnant or who is intending to become pregnant (self reported) over the duration of the study.

2. BREAST-FEEDING
A woman who is breast-feeding.

3. CONCURRENT MEDICATION/ MEDICAL HISTORY
a. Implanted with a cardiac pacemaker. b. Daily doses of medication that might interfere with the ability to perform the study according to protocol (as determined by the Investigator). c. Taking or have taken a bisphosphonate drug (i.e. Fosamax®, Actonel®, Boniva®) for treatment of osteoporosis.

d. A serious chronic disease requiring hospitalization..
e. Any condition not previously mentioned that in the Investigator's opinion may impair the study evaluation.

4. ALLERGY/ INTOLERANCE
Known or suspected intolerance or hypersensitivity to the study materials (or closely related compounds) or any of their stated ingredients.

5. DENTAL HEALTH / ORAL CONDITIONS
a. Any clinically significant or relevant oral abnormality (e.g. temporo-mandibular joint [TMJ] problems) that, in the opinion of the investigator, could affect the subject's participation in the study. b. Any subject clinically identified as having an incisal bite relation which could affect the bite force measurements. c. Severe dry mouth that may affect denture retention in the opinion of the Investigator. d. OST examination findings such as stomatitis, open sores, lesions, redness or swelling that, in the opinion of the investigator, could affect the subject's participation in the study.

6. CLINICAL STUDY/ EXPERMENTAL PRODUCT
a. Participation in another clinical study (including cosmetic studies) or receipt of an investigational drug within 30 days of the screening visit. b. Previous participation in this study.

7. SUBSTANCE ABUSE
Recent history (within the last year) of alcohol or other substance abuse.

8. LIFESTYLE
A subject who is unwilling to refrain from smoking, including e-cigarettes and the use of chewing tobacco or other tobacco products for the duration of screening and each treatment day (12-14 hours).

9. PERSONNEL
An employee of the sponsor or the study site or members of their immediate family.

4.3. Screening/ Baseline Failures

Screen failures are defined as subjects who consent to participate in the study but are never subsequently randomized. In order to ensure transparent reporting of screen failure subjects, a minimal set of screen failure information is required including Demography, Screen Failure details, Eligibility Criteria, and any Serious Adverse Events. Re-screening of subjects will not be allowed in this study.

4.4. Withdrawal/ Stopping Criteria

A subject may withdraw from the study at any time at his/her own request, or may be withdrawn at any time at the discretion of the investigator for safety, behavioural or administrative reasons.

If the reason for removal of a subject from the study is an AE or an abnormal laboratory test result, the principal specific event or test will be recorded on the electronic case report form (CRF). If a subject is withdrawn from the study because of a product limiting AE, thorough efforts should be clearly made to document the outcome. Any AEs ongoing at the final visit will be followed up until resolved, the condition stabilizes, is otherwise explained, or the subject is lost to follow-up.

The following actions must be taken in relation to a subject who fails to attend the clinic for a required study visit:

- The site must attempt to contact the subject and re-schedule the missed visit as soon as possible.
- The site must counsel the subject on the importance of maintaining the assigned visit schedule and ascertain whether or not the subject wishes to and/or should continue in the study.
- In cases where the subject is deemed 'lost to follow up', the investigator or designee must make every effort to regain contact with the subject (where possible, at least 2 telephone calls). The contact attempt should be documented in the subject's record.
- Should the subject continue to be unreachable, only then will he/she be considered to have withdrawn from the study with a primary reason of "Lost to Follow-up".

4.5. Subject Replacement

Subjects who withdraw from the study post-randomization will not be replaced.

4.6. Subject and Study Completion

A completed subject is one who has completed all phases of the study including the follow-up visit.

The end of the study is defined as the date of the last subject's last visit.

5. PRODUCT INFORMATION

5.1. Study Product

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

	Test Product 1	Test Product 2	Reference Product	Negative Control
Product Name	Test adhesive 1 with a thin nozzle	Test adhesive 2 with a thin nozzle	Super Poligrip® Free Adhesive Cream (USA marketplace)	No adhesive
Product Formulation Code (MFC)	CCI	CCI	CCI	N/A
Dose	Continuous strips applied to upper denture as per the application instructions	Continuous strips applied to upper denture as per the application instructions	3 dabs for upper denture as per the product label application instructions	N/A
Route of Administration	Oral topical	Oral topical	Oral topical	N/A
Dosing Instructions	applied to clean dry denture fit surface in a pattern consistent with the application instructions	applied to clean dry denture fit surface in a pattern consistent with the application instructions	applied to clean dry denture fit surface in a pattern consistent with the product label application instructions	N/A

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

Name of Item	Purpose
Super Poligrip® Free Adhesive Cream (USA marketplace)	To stabilize the lower denture (apply 2 dabs to the lower denture [if required]; sufficient to retain the lower denture) as per the product label instructions
Oral B® Denture brushes	Standard brush to brush dentures
Polident® Dentu Crème Denture Cleansing Paste (USA)	Cleaning of dentures (adhesive removal)
Reprosil medium body impression material and mixer tips	Ancillary supplies to aid with study conduct
Nitrile Finger Cots	Covering transducer prongs
Kimtech Wipes	Assorted use
Small and Large Anti-Static Weighing Boats	Weighing and transporting dentures
Spatulas (Square Tips)	Spreading dental caulk on transducer prong
Nitrile Gloves (these may be supplied by the clinical site)	Covering hands

The site will supply Disposable Barrier Sleeves - to cover the transducer.

All test denture adhesive tubes, and the positive control adhesive, will be overwrapped and then labelled. The Super Poligrip® Free Denture Adhesive Cream will be supplied in its commercial tube. Samples will be overwrapped so as not to potentially bias subject response on the 'extrudability' question following bite force measures (question 6; Appendix III). A study label will be affixed to each tube.

All sundry items will be supplied in commercial packaging to be distributed by site staff as required throughout the study duration.

Care should be taken with the supplied study 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. Subjects should be instructed to not remove or deface any part of the study label during the 'extrudability' question following bite force measures (question 6; Appendix III).

The site will provide paper copies of any study instructions and questionnaires.

® Oral B is a registered trademark of Procter & Gamble.
® Polident Dentu Crème is a registered trademark of GlaxoSmithKline Consumer Healthcare, LLC.

5.2. Dose Schedule

The denture adhesives will be applied by the Site Study Staff to a clean and dry upper complete denture following the pre-treatment baseline bite force measurement in accordance with the product Application Instructions (Appendix V & VI).

For adhesive test arms: A total of 1±0.05 gram (weighed) of denture adhesive will be applied to the dry maxillary denture in a pattern consistent with the product label and application instructions (Appendix V & VI). For all subjects in all arms: Super Poligrip® Free denture adhesive cream will be applied to the dry mandibular denture (if applicable) in a pattern consistent with the instructions on the product label.

Clean and dry upper complete dentures will be weighed and their masses recorded prior to and immediately following adhesive application for all products. The masses of the adhesives used will be calculated as the difference in the recorded masses pre- and post-adhesive application.

All application of denture adhesive should be made in an area not accessible by the examiner performing the bite force and OST (safety) assessment in order to ensure that the examiners remain blind. The denture will then be returned to the subject who should reposition the denture in their mouth. For subjects on the "no adhesive" treatment visit, the denture should be cleaned and dried as above, and then refitted by the subject, no weighing of the denture is necessary.

As stabilisation of the lower denture is necessary for accurate Bite Force measurements to be performed, reapplication of denture adhesive (to the lower denture only) may be performed up to a maximum of 2 times is acceptable on any given test day provided that; (1) the investigator deems it necessary for Bite Force measurements (2) the subject has been compliant with the protocol and has not actively washed the adhesive out.

5.3. Dose Modification

No dose modification is permitted in this study.

5.4. Product Compliance

The adhesive will be applied to dentures by one member of the study staff therefore excellent compliance is anticipated.

5.5. Precautions

No precautions will be necessary as product will be applied professionally as per marketed product label and the test denture adhesive application instructions (Appendix V & VI).

5.6. Overdose

An overdose is a deliberate or inadvertent administration of a product at a dose higher than specified in the protocol.

Overdose is not likely to occur in this study as product will be applied by a single member of staff. Limited quantities of the product will be supplied, and closely monitored by the site for each subject.

Overdose per se is not an AE. However, any clinical sequelae of an overdose should be reported as an AE (and serious adverse event (SAE), if appropriate). For reporting, follow the AE and SAE reporting instructions.

5.7. Rescue Therapy

No rescue therapy is required in this study.

5.8. Product Assignment

Subjects will be assigned to a specific study product order. Subjects will use each of the study products using this pre-determined randomised schedule. The randomization schedule will be generated by the Biostatistics Department, GSKCH, prior to the start of the study, using a validated internal procedure.

5.8.1 Randomization

A unique screening number will identify each subject screened for study participation. Screening numbers will be assigned in ascending numerical order as each subject signs their consent form. Subjects who meet all inclusion and exclusion criteria will be randomized according to the randomization schedule. Randomization numbers will be assigned in ascending numerical order as each subject is determined to be fully eligible.

The randomization schedule will indicate the treatment order sequence; one of the four treatments to be used for each of the four treatment periods. This randomisation will use a Williams Square layout and be provided by the Biostatistics Department, GSKCH. The study site will receive two randomization schedules, one with treatment de-codes and one without. The schedule without the treatment decodes will be used to

dispense study treatments to the subjects and the schedule with treatment decodes will be provided in a sealed envelope and will be available for emergency use only.

5.8.2 Blinding

The examiner, the study statistician and other employees of the Sponsor who may influence study outcomes are blinded to the product allocation of subjects. All study staff other than the member of Site Study Staff applying treatment will be blinded. The treatments will be applied and the denture will be fitted to the subject's mouth in a secluded area to preserve the blinding. The subject will be instructed not to disclose to the examiner whether or not treatment was applied. Access to aspects of the eCRF that are considered at risk of unblinding will be restricted where required in order to maintain study blinding.

5.8.3 Code Breaks

The blind must only be broken in an emergency where it is essential to know which product a subject received in order to give the appropriate medical care. Wherever possible the Investigator (or designee) must contact the Sponsor prior to breaking the blind. The investigator must document the reason for breaking the code and sign and date the appropriate document.

At the end of the study, this sealed randomization envelope with treatment decodes will be returned to the study sponsor.

5.9. Packaging and Labelling

The contents of the label will be in accordance with all applicable regulatory requirements and will be the responsibility of the Clinical Supplies Department, GSKCH.

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. Subjects should be instructed to not remove or deface any part of the study label.

Each study label will contain, but not be limited to, protocol number, product code letter (for treatment products only), directions for storage, emergency contact telephone number and "For Clinical Trial Use Only". In addition, the USA device warning "Caution: Investigational Device – Limited by Federal (or United States) Law to Investigational Use" will also be included on all labels.

5.9.1. Accountability of Product

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

The investigator or designee will maintain a full record of study product accountability. A Product Dispensing Log must be kept current and will contain the following information:

- The identification of the subject to whom the study product was dispensed.
- The date(s) and quantity of the study product dispensed to the subject.
- The date(s) and quantity of the study product returned by the subject (if applicable).

The inventory must be available for inspection by the study monitor during the study. At the end of the study, study product supplies will be verified by the monitor. Study product supplies will then be either collected by the study monitor or returned by the investigator or designee to the GSKCH Clinical Supplies Department or designated vendor.

5.9.2. Storage of Product

Study product supplies must be stored in compliance with the label requirements in a secure place with limited or controlled access.

6. STUDY ASSESSMENTS AND PROCEDURES

This section lists the procedures and parameters of each planned study assessment. The exact timing of each assessment is listed in the Schedule of Events section.

Adherence to the study design requirements, including all assessments and procedures are essential and required for study conduct.

6.1. Visit 1 - Screening Visit

6.1.1 Telephone Screening

Prior to the screening visit, telephone screening of interested subjects may be conducted using a telephone script. This will be conducted by the site recruitment staff or designee.

6.1.2. Informed Consent

The investigator, or designee, must obtain written (signed and dated by the subject) informed 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 any time. Appropriate forms for documenting written consent will be provided by the investigator or by GSKCH. 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 should be provided with a copy of the signed and dated amended consent form.

6.1.3. Demographics

The Investigator, or designee, will record each subject's year of birth, gender and race. In accordance with FDA guidelines (Guidance for Industry: Collection of Race and Ethnicity Data in Clinical Trials, 2005, FDA) the ethnicity of subjects will also be captured.

6.1.4. Medical History and Concomitant Medication

For each subject, the medical history will be taken and reviewed by the Investigator or medically qualified designee. Details of any relevant medical or surgical history, including allergies or drug sensitivity, will be recorded in the CRF. Any concomitant therapy taken in the 30 days prior to the Screening Visit and throughout the study will also be recorded in the CRF.

6.1.5. Dental History

The Investigator, or medically qualified designee, will take a dental history from each subject and recorded in the CRF. Dental history will include information of all prostheses in the mouth, maxillary and mandibulary, as well as information regarding the age of the dentures, and how long the subject has worn dentures. Documentation of prosthetic teeth material will also be recorded by the Investigator in the CRF.

6.1.6. Well-Made Denture Assessment

The examiner will examine each subject's denture in the maxilla and mandible (if present) to determine if he/she considers it to be well made i.e.:

- Denture(s) has adequate vertical dimension, freeway space, horizontal occlusal relationships and border extension
- Denture(s) has acceptable contour and finish
- Denture(s) has acceptable porosity, tissue surfaces, polished surfaces, color and thickness.

For each denture, maxillary and mandibular, if present, the examiner will identify from what material it is made and indicate acceptable or unacceptable on the CRF.

6.1.7. OST Examination – Edentulous

The OST Exam-Edentulous will include the maxillary mucogingival fold, maxillary edentulous gingival mucosa, maxillary hard palate, mandibular mucogingival fold, mandibular edentulous gingival mucosa (if applicable), gingival mucosa (if applicable), labial mucosa (including lips), buccal mucosa, tongue, sublingual area, soft palate, submandibular area, salivary glands, tonsilar 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. Adverse events will be assessed from the first OST examination at screening.

A single examiner should complete this assessment for all the subjects. If this is not possible, then the same examiner should perform this procedure for the same subject for all the visits.

6.1.8. Denture Bearing Tissue Score

The denture bearing tissue score (Kapur 1967) will be assessed by the investigator and recorded for the maxillary denture only on the appropriate CRF. There are no eligibility requirements associated with this measure in this bite force trial.

* Note, for completeness, the entire index (for maxillary and mandibular arches) is presented below. Due to an inconsistency observed in the original printed publication, the two descriptors below marked by an asterisk (*) have been modified (by inverting their order) to better reflect the authors intent and align with the grading scale.

Ridge Shape (for both Maxillary and Mandibular)

1= Flat
2= V-shaped
3= Shaped between U and V
4= U shaped

Tissue Resiliency (for both Maxillary and Mandibular)

1= Flabby
2= Resilient
3= Firm

Location of Border Tissue Attachment

Maxillary Arch	Mandibular Arch
1= Low	1= High
2= Medium	2= Medium *
3= High	3= Low *

6.1.9. Kapur (Olshan Modification) Denture Retention & Stability Assessment

At the screening visit, the examiner will determine the subject's denture retention and stability score and it will be recorded in the CRF.

Retention Criteria

With gloved hands, the examiner will attempt to unseat the maxillary complete 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 Criteria

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 maxillary complete 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

Following completion of informed consent (section 6.1.2), medical history/ concomitant medication (section 6.1.4), dental history (section 6.1.5), well-made denture assessment (section 6.1.6), OST examination (section 6.1.7) and Kapur index/ assessment (section 6.1.9), subject inclusion/ exclusion will be determined as per the inclusion/ exclusion criteria (section 4).

6.1.10. Denture cleansing

Dentures should be removed from the mouth by the subject. Denture cleansing should be performed by suitably qualified site staff. Enough denture cleansing paste will be applied to the supplied denture brush. Holding the upper (and lower where necessary) all surfaces of the dentures will be thoroughly cleaned to remove all traces of denture fixative, plaque and particulates/debris. The dentures will then be rinsed thoroughly with running water. Dentures should then be dried using clinical paper towels prior to denture adhesive application. Please note that the denture cleansing paste is to be used extra-orally and not for use in the mouth. Hands should be washed thoroughly following application and use of the denture cleansing paste.

6.1.11. Mandibular Denture Stabilisation

Prior to all bite force measures, if deemed necessary at the discretion of the Investigator in order to ensure accuracy of bite force measures, any lower denture (partial or complete) will be fully stabilized by the investigator using the positive control denture adhesive (Super Poligrip® Free Adhesive Cream). This will be completed, when necessary, for all screening, practice, training and test bite force measurements.

6.1.12. Bite Force Measures prior to and at Screening

A bite force transducer system will be supplied by GSKCH and used to measure incisal bite force needed to dislodge the maxillary denture. The transducer system is composed of two plates embedded with a strain gauge that measures displacement of the upper denture during biting.

Each subject will have their bite force assessments with the same examiner. In this way inter-examiner variability will be minimized. Bite force data will be recorded on the appropriate CRF page.

6.1.13. Bite Force Calibration

The bite force device will be calibrated using appropriate software or through the application of incremental forces to the transducer by GSKCH's external vendor Specialty Measurements Incorporated (SMI), in agreement with GSK staff and the investigator prior to commencing the study. A Certificate of Calibration (which lasts for 12 months) will be provided before the start of the study and filed within the site's Regulatory Binder and the Study Master File.

6.1.14. Bite Force Measures at Screening

At Screening, subjects will have any denture adhesive on their denture removed. A member of site staff (trained in bite force procedures) will instruct the subjects in the execution of the bite force procedure participation. The subject will be instructed to sit and hold his/her head in a natural position so that the occlusal plane is parallel to the floor. The examiner will stand or sit in front of the subject holding the bite force transducer parallel to the floor at a comfortable level for the subject. In order to facilitate insertion the examiner may angle the bite force plates for certain subjects as necessary. The examiner will prevent cross contamination by placing a clean finger cot over the bite force plates for each subject in addition to a clean infection control sleeve over the transducer hand piece. The examiner will insert the bite force plates into the subject's mouth, which may be customized using impression material in

order to facilitate anterior denture tooth placement on the bite force transducer. The examiner will instruct the subject to swallow, and then ensure that the muscles of mastication are relaxed. The examiner will signal the subject to bite until he/she feels movement on the maxillary denture at which time he/she will be instructed to release the bite plate. If, in the opinion of the examiner, the subject will be unable to successfully complete the required bite force system training tasks, the subject will be withdrawn from the study.

During the Screening Visit, the examiner will record a triplicate bite force measurement at pre-treatment baseline without denture adhesive. These will be referred to as "training bites" on the CRF as the subject becomes accustomed to the equipment. Four (4) further bites will be made; 2 of these 4 'qualifying' bites must be reproducible (±2lb) for a subject to be eligible to the study. All 4 of the "qualifying" bites must be less than or equal to 9 pounds. These will form the subject eligibility/ adherence for continuation in the study.

6.2. Visits 2, 3, 4 & 5

6.2.1. OST Examination - Edentulous

Full OST edentulous assessments will be performed by the investigator twice during each of the Test Days; at pre-treatment baseline and also at the end of each of the Test/Treatment Visits. OST examinations will be performed as previously outlined in Section 6.1.7.

6.2.2. Denture Adhesive Application to Dentures

Prior to denture adhesive application, Denture Cleansing (Section 6.1.10) will be performed as previously described. Denture adhesive will be applied to the dentures by a suitably qualified member of site staff (blinded to the investigator collecting efficacy measures) as per the Denture Adhesive Application Instructions (Appendix V & VI). Upper dentures shall be weighed before and after adhesive application, and weights (including weight of adhesive used) recorded in the eCRF to ensure correct dose applied (1±0.05 grams). The specific tube used for denture adhesive application will be retained for use to assess product extrusion (Appendix III, question 6) to prevent the risk of cross-infection.

6.2.3. Bite Force Measures during Treatment Visits

Prior to Bite Force measures during each of the treatment visits, Denture Cleansing (Section 6.1.10) and Mandibular Denture Stabilisation (Section 6.1.11) will be performed as previously described.

On each treatment day, the examiner will record triplicate bite force measurements without denture adhesive. These three measurements will be referred to as "practice bites", where the goal is to have the subject re-familiarize themselves with the system. The 4th bite of the series will be captured as the Test Day pre-treatment baseline bite force. Test Day bite force readings must be within (±2 lb) for 1 of the 3 "practice bites" and the pre-treatment baseline bite. In addition, only subjects whose test day pre-treatment baseline bite force is less than or equal to 9 pounds will be eligible to proceed. If a subject does not meet these criteria at any test day visit they will be discontinued entirely from the study. Additional bite force measures will take place 0.5 (immediately prior to completion of product ooze questionnaire) followed by 1, 3, 6, 9 and 12 hours after application of each test adhesive (or no treatment as per the randomization schedule).

At each post-adhesive time-point, the subject will swallow and then bite on the transducer until the maxillary denture dislodges. No post adhesive application bite force measurements will be made earlier than the specified time and not later than 5 minutes after the specified time. Bite force data will be recorded on the appropriate CRF. ~~Incidents will be assessed pre- and post-bite force recordings on each of the treatment days.~~

6.2.4. Subject Questionnaires

These questionnaires will only be completed by the subjects during treatment visits where subjects are assigned to adhesive.
A questionnaire pertaining to product ooze will be completed by the subjects immediately after the 0.5 hrs bite force measurement (Appendix II). Furthermore, a questionnaire regarding sensory attributes around flavour and texture will be completed immediately after completion of the 12 hrs bite force measurement whilst the upper denture is still retained in the mouth (Appendix III). Completion of this questionnaire will also involve the subject extruding some denture adhesive onto paper prior to answering the question regarding ease of product extrusion (question 6; Appendix III). A third and final denture removal questionnaire will be completed immediately following the 12 hrs bite force measurement, following completion of the sensory questionnaire and removal of the upper denture from the mouth by the subject (Appendix IV). This final "denture removal questionnaire" (Appendix IV) must be reviewed by Study Staff immediately following completion whilst the subject is still present, in order to ensure that any potential AEs that may be included in the free text (question 3; Appendix IV) are investigated by Study Staff and captured in the eCRF.

All questionnaires will be completed by the subjects according to the study schedule (i.e. when undertaking the treatment, but not the no-treatment negative control study arms) in a quiet environment without external influence. Subjects will not be issued a questionnaire when completing the 'no adhesive' negative control treatment arm. The study Investigator(s) (in particular all site study staff involved in the collection of bite force and OST data) will remain blinded to the distribution and completion of all questionnaires. All questionnaire data will be captured in the eCRF, and will be monitored on site in order to ensure that all patient reported outcomes are captured in the database, paying particular attention to the free text about denture adhesive likes & dislikes (question 2; Appendix IV).

6.2.4. Study Conclusion

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 CRF by selecting one of the options below.

a) Subject did not meet study criteria

b) Adverse Event/ SAE or Incident

c) Lost to Follow Up

d) Protocol Violation

e) Withdrawal of Consent

f) Other

7. SAFETY ASSESSMENTS

7.1. Definitions of an Adverse Event and Serious Adverse Event

7.1.1. Adverse Events

The investigator or site staff will be responsible for detecting, documenting and reporting events that meet the definition of an AE or SAE.

Adverse Event Definition:
• An AE is any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with the use of an investigational

or washout product, whether or not considered related to the investigational or washout product.

- NOTE: An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of an investigational or washout product.

Events meeting AE definition include:

- Any abnormal laboratory test results (if applicable) or other safety assessments, including those that worsen from baseline, and felt to be clinically significant in the medical and scientific judgment of the investigator.
- Exacerbation of a chronic or intermittent pre-existing condition including either an increase in frequency and/or intensity of the condition.
- New condition(s) detected or diagnosed after study product administration even though it may have been present prior to the start of the study.
- Signs, symptoms, or the clinical sequelae of a suspected interaction.
- Signs, symptoms, or the clinical sequelae of a suspected overdose of either study product or a concomitant medication (overdose per se will not be reported as an AE/SAE).

Events NOT meeting definition of an AE include:

- 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/ condition 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): the condition that leads to the procedure is an AE.
- 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.

7.1.2. Serious Adverse Events

Serious Adverse Event is defined as any untoward medical occurrence that, at any dose:

A. Results in death

B. Is life-threatening
NOTE: The term 'life-threatening' in the definition of 'serious' refers to an

event in which the subject 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.

C. Requires hospitalization or prolongation of existing hospitalization

NOTE: In general, hospitalization signifies that the subject 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 out-patient setting. Complications that occur during hospitalization are AEs. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred or was necessary, the AE should be considered serious.

Hospitalization for elective treatment of a pre-existing condition that did not worsen from baseline is not considered an AE.

D. Results in disability/incapacity

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

E. Is a congenital anomaly/birth defect

F. Other Situations

- Medical or scientific judgment should be exercised in deciding whether reporting is appropriate in other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the subject or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These should also be considered serious.
- Examples of such events are 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 hospitalization or development of drug dependency or drug abuse or reports of spontaneous abortion.

7.2. Recording Adverse Events and Serious Adverse Events

Recording of adverse events and serious adverse events:

- The investigator or site staff will be responsible for detecting, documenting and reporting events that meet the definition of an AE or SAE.

- The investigator or site staff will then record all relevant information regarding an AE/SAE in the CRF.
- 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 of 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).
- AEs will be collected from the **OST EXAMINATION AT SCREENING** ~~beginning of the Screening Visit~~ and until 5 days following last administration of the study product.
- SAEs will be collected over the same time period as stated above for AEs. However, any 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 consents to participate in the study up to and including any follow-up contact.
- Medical conditions reported prior to the time period for reporting AEs/SAEs should be recorded as part of the subject's medical history.

7.3. Evaluating Adverse Events and Serious Adverse Events

Assessment of Intensity:

The investigator or designee will make an assessment of intensity 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. - an AE that is assessed as severe will not be confused with an SAE. Severity is a category utilized for rating the intensity of an event; and both AEs and SAEs can be assessed as severe.

Note: An event is defined as 'serious' when it meets at least one of the pre-defined outcomes as described in the definition of an SAE.

Assessment of Causality:

- The investigator is obligated to assess the relationship between study product and the occurrence of each AE/SAE.

- A "reasonable possibility" is meant to convey that there are facts/evidence or arguments to suggest a causal relationship, rather than a relationship cannot be ruled out.
- The investigator will use clinical judgment to determine the relationship.
- Alternative causes, such as natural history of the underlying diseases, concomitant therapy, other risk factors, and the temporal relationship of the event to the study product will be considered and investigated.
- The investigator will also consult the Investigator Brochure (IB) and/or Product Information, for marketed products, in the determination of his/her assessment.
- For each AE/SAE the investigator **must** document in the medical notes (source document) or CRF that he/she has reviewed the AE/SAE and has provided an assessment of causality.
- 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, amending the SAE data collection tool accordingly.
- The causality assessment is one of the criteria used when determining regulatory reporting requirements.

7.4. Reporting Adverse Events and Serious Adverse Events

AE Reporting to GSKCH:

- AEs will be recorded in the AE section of the CRF.
- Medical conditions recorded by the subject on a diary card or similar document that meet the definition of an AE must also be recorded in the AE section of the CRF, if not previously well-characterized by the investigator in 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. The investigator or designee must ask the subject the following question during each visit including any follow-up visits: ***"Have you felt unwell, experienced any symptoms or taken any medication (since your last visit) (today) (since your last dose) (since the last session)?"***
- The medically qualified investigator should review adverse events in a timely manner; this review should be documented in writing in the source document or in the CRF.
- After the study is completed at a given site, and the site has received their study data on Compact Discs (CDs), the electronic data collection tool will be removed from the internet to prevent the entry of new data or changes to

existing data.

SAE Reporting to GSKCH:

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:

- Protocol and subject identifiers
- Subject's demography
- Description of events, with diagnosis if available
- Investigator opinion of relationship to study product (see section 8.3)
- Criterion for seriousness.

The following are desirable and are of particular relevance for investigator and GSKCH 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, and SAE fax cover sheet must be faxed or e-mailed to the appropriate GSKCH Study Manager as soon as possible, **but not later than 24 hours** after study site personnel learn of the event. The GSKCH Study Manager should be notified of the situation by telephone or email.

Fax Serious Adverse Events to:
US: PPD

The GSKCH Study Manager will be responsible for forwarding the SAE form to the Case Management Group, Global Clinical Safety and Phamacovigilance, the Medical Director responsible for the study and other GSKCH personnel as appropriate via email.

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

7.5. Follow-up of Adverse Events and Serious Adverse Events

Follow-up of AEs and SAEs:

- 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 stabilizes,

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

Regulatory and ethics reporting requirements for SAEs:

- The investigator will promptly report all SAEs to GSKCH within the designated reporting timeframes (within 24 hours of learning of the event). GSKCH 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 notification of SAEs by the investigator to GSKCH is essential so that legal obligations and ethical responsibilities towards the safety of subjects are met.
- GSKCH will comply with country specific regulatory requirements relating to safety reporting to the regulatory authority, IRB and investigators.
- Investigator safety reports are prepared according to GSKCH policy and are forwarded to investigators as necessary. An investigator safety report is prepared for a SAE(s) that is both attributable to investigational product and unexpected. The purpose of the report is to fulfill specific regulatory and GCP requirements, regarding the product under investigation.
- An investigator who receives an investigator safety report describing a SAE(s) or other specific safety information (e.g., summary of listing of SAEs) from GSKCH will file it with the Investigator Brochure (or safety statement) and will notify the IRB , if appropriate according to local requirements.

7.6. Definition of and Procedure for Reporting Medical Device Incidents

Medical devices are being provided by GSKCH for use in this study; the medical devices in this study are the denture adhesives, the denture cleaning brushes and denture cleansing paste. GSKCH medical device incidents, including those resulting from malfunctions of the device, must be detected, documented, and reported by the investigator on the CRF throughout the study.

7.6.1. Definition of an Incident

Definition of an Incident:
• 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 lead to the death of a patient or user or of other persons or to a serious deterioration in their state of health.

7.6.2. Reporting of Incidents and Malfunctions

Incident Reporting to GSKCH:

- **All incidents must be reported to GSKCH 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.
- The Incident Report Form will be completed as thoroughly as possible and signed by the investigator before transmittal to GSKCH. 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 faxed or emailed to the appropriate GSKCH Study Manager 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 GSKCH Study Manager should be notified of the situation by telephone or email.

Fax the Incident Report Forms to:
US: PPD

- The GSKCH Study Manager will be responsible for forwarding the Incident Report Form to the Case Management Group, Global Clinical Safety and Pharmacovigilance, the Medical Director responsible for the study and other GSKCH personnel as appropriate.

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

Reporting of Malfunctions to GSKCH:
The investigator will follow the following directions regarding device failure (malfunction): • Notify GSKCH immediately. • 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.

7.6.3. Follow-up of Incidents

Follow-up of Incidents:
During the study: • All incidents will be followed until resolution of the event, until the condition stabilizes, until the condition is otherwise explained, or until the subject is lost to follow-up. This applies to all subjects, including those withdrawn prematurely. The investigator is responsible for ensuring that follow-up includes any supplemental investigations as may be indicated to elucidate as completely as practical the nature of the incident. • New or updated information will be recorded on the originally completed form with all changes signed and dated by the investigator. After the study: • Investigators are not obligated to actively seek reports of incidents in former subjects. However, if the investigator learns of any incident at any time after a subject has been discharged from the study, and such incident is reasonably related to a GSKCH medical device provided for the study, the investigator will promptly notify GSKCH.

Regulatory and Ethics Reporting Requirements for Incidents:
• The investigator will promptly report all incidents occurring with any GSKCH medical device provided for use in the study within 24 hours. GSKCH has a legal responsibility to notify appropriate regulatory bodies and other entities about certain safety information relating to medical devices being used in clinical studies. Prompt notification of incidents by the investigator to GSKCH is essential in order to meet legal obligations and ethical responsibility towards the safety of subjects. • The investigator, or responsible person according to local requirements, will comply with the applicable local regulatory requirements relating to the reporting of incidents to the IRB.

7.7. Collection of Pregnancy Information

7.7.1. Time Period for Collecting of Pregnancy Information

Collection of Pregnancy Information:
• Pregnancy information will be collected on all pregnancies reported following administration of any investigational product. Information on pregnancy identified during the screening phase and prior to investigational product administration does not need to be collected.

7.7.2. Action to be Taken if Pregnancy Occurs

Action to be Taken:
• The investigator will collect pregnancy information on any subject who becomes pregnant while participating in the study after administration of the investigational product. The investigator will record pregnancy information on the appropriate form and submit it to GSKCH within 2 weeks of learning of the subject becoming pregnant. 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 to GSKCH. 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, any pregnancy complication or elective termination for medical reasons will be recorded as an AE or SAE. • A spontaneous abortion is always considered to be an SAE and will be reported as such. An SAE occurring in association with a pregnancy, brought to the investigator's attention after the subject completed the study and considered by the investigator as possibly related to the investigational product, must be promptly forwarded to GSK. • While the investigator is not obliged to actively seek this information in former study participants, he or she may learn of an SAE through spontaneous reporting. • For non-medicinal or licensed products with no pregnancy warning on the label, use the following text: "There is no requirement for the subject to be withdrawn from the study as a result of the pregnancy. However if they are withdrawn, this should be recorded in the appropriate section of the CRF."

8. DATA MANAGEMENT

For this study subject data will be entered into an electronic case report form, using a GSKCH validated data system.

8.1. 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 the Source Document Designation Form. In some cases the CRF can be used as a source document.

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

8.2. Electronic 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 authorized designee) to certify that the data are complete and correct.

Management of clinical data will be performed in accordance with applicable GSKCH standards and data cleaning procedures to ensure the 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 birth date) is to be recorded in the CRF or as part of the query text.

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

Subject data will be entered into GSKCH defined CRFs and transmitted electronically to GSKCH in a validated (21 CFR Part 11 compliant) web-based electronic data capture system (InForm™).

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.

The CRFs (including queries, query responses and audit trails) will be retained by GSKCH. Site data archived compact discs (CD(s)) prepared by a third party will be sent to the investigator to maintain as the investigator copy following the decommissioning of the study.

8.3. 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.

8.3.1. Data 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) are reported 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. Monitor can also run reports and listings on the CRFs, to raise manual queries as needed for site clarification or correction

8.4. Processing Patient Reported Outcomes

Patient reported outcome (PRO) data are collected directly from the subject PRO measures e.g. diary cards, questionnaires etc, and entered into the sponsor's clinical data management system (DMS) by the study site representative. In instances where the PRO data is entered into the DMS by GSKCH, the PROs will be anonymised, and forwarded to GSKCH for entry, as agreed and documented ahead of the study starting. PROs that are source will be retained by the investigator and certified copies will be sent to GSKCH.

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 GSKCH.

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

9. STATISTICAL CONSIDERATIONS AND DATA ANALYSES

9.1 Sample Size Determination

Approximately 25 subjects will be screened to randomize approximately 21 subjects to ensure that approximately 18 evaluable subjects complete the study.

A sample size of approximately 18 subjects completing all treatment periods will provide approximately 81% power to detect a difference of 2.01 lbs in at least one of the two test products from no adhesive, using two-sided t-tests with family wise significance level of 5% based on the Dunnett's adjustment, assuming a residual standard deviation of 1.929 lbs. The estimate of SD is obtained from the study 203114. This was the larger SD among two similar earlier studies: RH02625 and 203114. The delta of 2.01 was obtained from the study RH02443. In that study this was the observed difference between Super Poligrip and no adhesive. This was the lowest observed delta for Super Poligrip vs no adhesive among the studies RH02446, RH02443 and 203114. As such the expected performance of the test products is completely unknown but we would like at least one test product to perform like Super Poligrip or better.

Power calculations were performed for 2 alternative hypotheses:

1. One of the treatment means is 2.01 lbs more than the mean for no adhesive; the other treatment mean is 1 lb more than the mean for no adhesive

2. One treatment mean is 2.01 lbs more than the mean for no adhesive; the other treatment mean is the same as the mean for no adhesive.

The power was approximately 81% for both the cases.

The results are based on 100000 simulations.

9.2. General Considerations

9.2.1. Definition of Analysis Populations

All analyses of safety will be made on the safety population which will be defined as all subjects who are randomized and received treatment at least once during the study. The safety population will be analyzed as per treatment received (ATRT variable).

Efficacy analyses will be based on the intent-to-treat (ITT) population which will be defined as all randomized subjects with at least one post baseline assessment of efficacy. This will be the primary population for the efficacy analysis which will be performed as per the randomized treatment.

The Per Protocol (PP) population will be a subset of the ITT population. Subjects with a protocol violation that is deemed to affect efficacy assessments in all study periods will be excluded from the PP population. Subjects with a protocol violation that is deemed to affect efficacy assessments in some (but not all) study periods will be part of the PP population, but their data will be excluded from the period(s) affected by the protocol violation for a PP analysis. An analysis on the PP population will be performed for the primary efficacy variable if there is more than 10% difference in the number of subjects evaluable in any of the treatment groups for the ITT and PP populations. A decision on whether a PP analysis will be performed will be made prior to study unblinding.

9.2.2. Exclusion of Data from Analysis

No data will be excluded from the safety or ITT populations.

The following will be considered violations that may lead to the exclusion of data for PP analysis:

- Violation of inclusion or exclusion criteria at screening that may affect efficacy
- Violation of pre-treatment baseline bite force continuance criteria
- Treatment administration errors
- Use of prohibited treatment or medication before or during the study, which it is felt will affect the assessment of efficacy

Other reasons for protocol violations may be provided in the Statistical Analysis Plan (SAP). Violations will be identified between the Biostatistician and Medical Director or designee, ahead of breaking the study blind. Further details of methodology for identifying data to be included in PP analysis will be provided in the SAP.

9.2.3. Criteria for Evaluation

9.2.3.1. Criteria for Assessing Efficacy

Efficacy will primarily be assessed by Area Over Baseline (AOB) over 12 hours for the incisal bite force (lbs) (denoted by AOB_{0-12}). The difference will be estimated for each of the test products compared to no adhesive.

Success would be achieved if any of the test products was statistically significantly better than no adhesive. The observed differences for the treatment means will also be considered.

9.2.3.2. Criteria for Assessing Tolerability

The assessment for safety will be based on the OST examination and adverse events (AEs) and incidents reported by subjects following application of denture adhesives.

9.2.4. Handling of Dropouts and Missing Data

For calculation of AOB, linear interpolation will be used in the case of missing values. If more than one of the assessments during the 12 hour period is missing, AOB will be set to missing.

9.3. Statistical Methods and Analytical Plan

More details of the proposed statistical analysis will be documented in the statistical analysis plan, which will be written following finalisation of the protocol and prior to study unblinding.

Selected raw data will be listed as defined in the SAP.

9.3.1. Demographic and Baseline Characteristics

Descriptive statistics (number of subjects, mean, SD, median, minimum and maximum for continuous variables, and frequency and percentage for categorical variables) will be provided for demographic and baseline data.

9.3.2. Primary Analysis(es)

Incisal Bite Force (lbs): Area over Baseline (AOB_{0-12})

The Area Over Baseline (AOB) over 12 hours for the incisal bite force (lbs) (denoted by AOB_{0-12}) is the primary efficacy variable.

To calculate this variable first the Area Under the Curve (AUC) is calculated from 0 to 12 hours (AUC_{0-12}) using the trapezoidal method. AOB_{0-12} will be calculated as (AUC_{0-12})/12 minus baseline bite force (lbs). This transformation will return the measurement to the same scale as the original observations whilst also looking at the average amount of improved force over time by subtracting the baseline value (AOB: Area Over Baseline). Higher values of AOB demonstrate a stronger bite force over time than lower values.

Missing readings will be ignored and interpolation will be made between pre and post the missing values, if necessary. In the case of more than one missing value or if the 12 hour value is missing, the AOB will be set to missing.

An analysis of covariance (ANCOVA) model will be used with AOB values as the response, with fixed effect factors for treatment group, period and subject-level baseline, period level baseline minus subject-level baseline as covariates. Subject will be included as a random effect.

From the above model, treatment differences between groups, (each of the two adhesives versus no adhesive), 95% confidence intervals and p-values, will be provided. The confidence intervals and p-values will be adjusted using the Dunnett's method so that the overall confidence level for the two confidence intervals is maintained at 95% and the two treatment comparisons can be performed with an overall 5% significance level. The assumption of normality and homogeneity of variance will be investigated. Violation of these assumptions may be overcome using suitable transformation or performing a non-parametric test (e.g. the Wilcoxon Sign Rank test).

9.3.3. Secondary Analysis(es)

Incisal Bite Force (lbs): Area over Baseline ($AOB_{0-0.5}$, AOB_{0-1}, AOB_{0-3}, AOB_{0-6}, AOB_{0-9}, AOB_{0-12})

From the ANCOVA model described above, treatment difference for each of the two test adhesives versus Super Poligrip® Free will be provided along with 95% confidence intervals and p-values. All tests will be conducted at the two sided 5% significance level. If non-parametric analysis is performed for the primary efficacy variable then these secondary comparisons will be performed in a similar way as the primary comparisons.

Further secondary efficacy variables will be bite force AOBs over 0.5, 1, 3, 6 and 9 hours respectively. Each of these secondary efficacy variables will be analysed using a similar ANCOVA model as described above for the primary efficacy variable.

From this model, treatment difference between each test adhesive versus Super Poligrip® Free, the treatment difference between each test adhesive versus no adhesive, 95% confidence intervals and p-values, will be provided. All significance tests will be conducted at the two sided 5% significance level. The assumption of normality and homogeneity of variance will be investigated. Violation of these assumptions may be overcome using suitable transformations or performing a non-parametric tests (e.g. the Wilcoxon Sign Rank test).

9.3.4. Exploratory/ Other Analysis(es)

For each ANCOVA model described above for each secondary efficacy variable, treatment difference between the two test adhesives will be provided along with 95% confidence intervals and p-values. All tests will be conducted at the two sided 5% significance level. If non-parametric analyses are performed for a secondary efficacy variable then this corresponding exploratory comparison will be performed in a similar way as the associated secondary comparisons for that secondary endpoint.

The data from the questionnaires and the denture adhesive weights will be listed and tabulated using descriptive statistics.

9.3.5. Safety Analysis(es)

Safety will be assessed based on any oral AEs (this includes those that are identified as Treatment Emergent OST abnormalities and spontaneously reported oral AEs). All AEs will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). AEs will be categorized as oral and non-oral by the clinical research director or designee prior to database lock. AEs will be deemed to be TE if they occur after the first supervised use of the randomized treatment. No formal statistical analyses of AEs will be performed. A list of incidents will also be included as part of the safety analyses.

10. STUDY GOVERNANCE CONSIDERATIONS

10.1. Posting of Information on Publicly Available Clinical Trials Registers

Study information from this protocol will be posted on publicly available clinical trial registers before enrollment of subjects begins.

10.2. Regulatory and Ethical Considerations, Including the Informed Consent

The study will be conducted in accordance with all applicable regulatory requirements, and with GSK policy.

As per the regulatory determination for this study, the experimental denture adhesive is categorized as a non-significant risk medical device, and therefore a non-significant risk (NSR) application will be required as part of the IRB submission to conduct this study in the US.

The study will also be conducted in accordance with ICH Good Clinical Practice (GCP), all applicable subject privacy requirements, and the guiding principles of the current version of the Declaration of Helsinki. This includes, but is not limited to, the following:

- Before initiating a trial, the investigator/institution should have written and dated approval/favorable opinion from the IRB for the trial protocol (including amendments), written informed consent form, consent form updates, subject recruitment procedures (e.g., advertisements), investigator brochure/ safety statement (including any updates) and any other written information to be provided to subjects. A letter or certificate of approval will be sent by the investigator to the sponsor prior to initiation of the study, and also when subsequent amendments to the protocol are made.
- Signed informed consent to be obtained for each subject before participation in the study (and for amendments as applicable)
- Investigator reporting requirements (e.g. reporting of AEs/SAEs/protocol deviations to IRB)
- GSK will provide full details of the above procedures, either verbally, in writing, or both.

10.3. Quality Control (Study Monitoring)

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 GSKCH. 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.

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

10.5. Conditions for Terminating the Study

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

Both GSKCH and the Investigator reserve the right to temporarily suspend or prematurely discontinue this study at any time for reasons including, but not limited to, safety or ethical issues or severe non-compliance. For multicenter studies (if applicable), this can occur at one or more or at all sites.

If the trial is prematurely terminated or suspended for any reason, the investigator site should promptly inform the trial subjects and should assure appropriate therapy/ follow-up for the subjects. Where required by the applicable regulatory requirements, GSKCH should inform the regulatory authority(ies).
In addition:

- If the investigator terminates or suspends a trial without prior agreement of GSKCH, the investigator site should promptly inform the sponsor and the IRB, and should provide the sponsor and the IRB a detailed written explanation of the termination or suspension.
- If the GSKCH terminates or suspends a trial, the investigator should promptly inform the IRB and provide the IRB a detailed written explanation of the termination or suspension.
- If the IRB terminates or suspends its approval/favorable opinion of a trial, the investigator should promptly notify the GSKCH and provide GSKCH with a detailed written explanation of the termination or suspension.

10.6. 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 GSKCH, 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 GSKCH, e.g. subjects' written consent forms, should be maintained by the investigator in strict confidence.

GSK will inform the investigator of the time period for retaining these records to comply with all applicable regulatory requirements (GSKCH recommends that documents be kept for 10 years). The investigator is also required to keep subject identification codes on file for at least 15 years after completion or discontinuation of the study. 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 GSKCH 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.

10.7. Provision of Study Results to Investigators, posting of Information on Publicly Available Clinical Trials Registers and Publication

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. REFERENCES

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12. APPENDICES

12.1. Appendix I - Abbreviations

Abbreviations

AE	Adverse Event
AOB	Area over baseline
CD	Compact Disc
CRF	Case Report Form
EDC	Electronic Data Capture
GCP	Good Clinical Practice
GSKCH	GlaxoSmithKline Consumer Healthcare
Hr	Hour
ICH	International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
IEC	Independent Ethics Committee
IRB	Institutional Review Board
ITT	Intention to Treat
OST	Oral soft tissue
PII	Personally Identifiable Information
PP	Per Protocol
PRO	Patient Reported Outcome
PVA	Polyvinyl acetate
SAE	Serious Adverse Event
US	United States of America

Trademark Information

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POLIGRIP

12.2. Appendix II – Product Ooze Questionnaire

Please note that this questionnaire is only completed for subjects on treatment visits when they have a denture adhesive applied and NOT on the no adhesive treatment visit.

Question 1 to be completed by the subject immediately after the 0.5 hour bite force reading.

Please mark/ tick only ONE response per question.

1. **How long after inserting your denture did you experience denture adhesive OOZING out of your UPPER DENTURE?**

Immediately	Less than approximately 10 minutes	Approximately 10 to 20 minutes	Approximately 20 to 30 minutes	No ooze experienced
☐	☐	☐	☐	☐
1	2	3	4	5

12.3. Appendix III – Sensory Questionnaire

Please note that this questionnaire is only completed for subjects on treatment visits when they have a denture adhesive applied and NOT on the no adhesive treatment visit.

To be completed by the subject immediately following the last (12 hr) bite force measure (whilst upper denture still retained in the mouth). Questions relate to the UPPER DENTURE only.

Please mark/ tick only ONE response per question.

1. **How would you rate your OVERALL OPINION of the denture adhesive?**

Dislike extremely	Dislike moderately	Dislike slightly	Neither like nor dislike	Like slightly	Like moderately	Like extremely
☐	☐	☐	☐	☐	☐	☐
1	2	3	4	5	6	7

2. **How much did you LIKE/ DISLIKE the TASTE of the denture adhesive?**

Dislike extremely	Dislike moderately	Dislike slightky	Neither like nor dislike	Like slightly	Like moderately	Like extremely
☐	☐	☐	☐	☐	☐	☐
1	2	3	4	5	6	7

3. How would you describe the STRENGTH of the TASTE of the denture adhesive?

No flavour at all	Barely detectable	Weak	Moderate	Strong	Very strong	Strongest flavour imaginable
☐	☐	☐	☐	☐	☐	☐
1	2	3	4	5	6	7

4. How much did you LIKE/ DISLIKE the FEEL of the adhesive in the mouth?

Dislike extremely	Dislike very much	Dislike moderately	Neither like nor dislike	Like moderately	Like very much	Like extremely
☐	☐	☐	☐	☐	☐	☐
1	2	3	4	5	6	7

5. How would you describe the TEXTURE of the denture adhesive?

	Not at all	Slightly	Moderately	Very	Extremely
Smooth	☐	☐	☐	☐	☐
Oily	☐	☐	☐	☐	☐

Gritty	☐	☐	☐	☐	☐
	1	2	3	4	5

For the following question subjects to be given a tube of the test product and asked to squeeze the adhesive on to a piece of paper as per the strips that appear on the product application

6. How EASY was it to SQUEEZE OUT the adhesive from the tube?

Not at all easy	Slightly easy	Moderately easy	Very easy	Extremely easy
☐	☐	☐	☐	☐
1	2	3	4	5

12.4. Appendix IV – Denture Removal Questionnaire

Please note that this questionnaire is only completed for subjects on treatment visits when they have a denture adhesive applied and NOT on the no adhesive treatment visit.

To be completed by the subject immediately after denture removal.

Please mark/ tick only ONE response per question.

1. **How EASY was it to REMOVE the denture from the mouth?**

Not at all easy	Slightly easy	Moderately easy	Very easy	Extremely easy
☐	☐	☐	☐	☐
1	2	3	4	5

2. **How EASY was it to REMOVE ANY RESIDUAL DENTURE ADHESIVE from the mouth?**

Not at all easy	Slightly easy	Moderately easy	Very easy	Extremely easy
☐	☐	☐	☐	☐
1	2	3	4	5

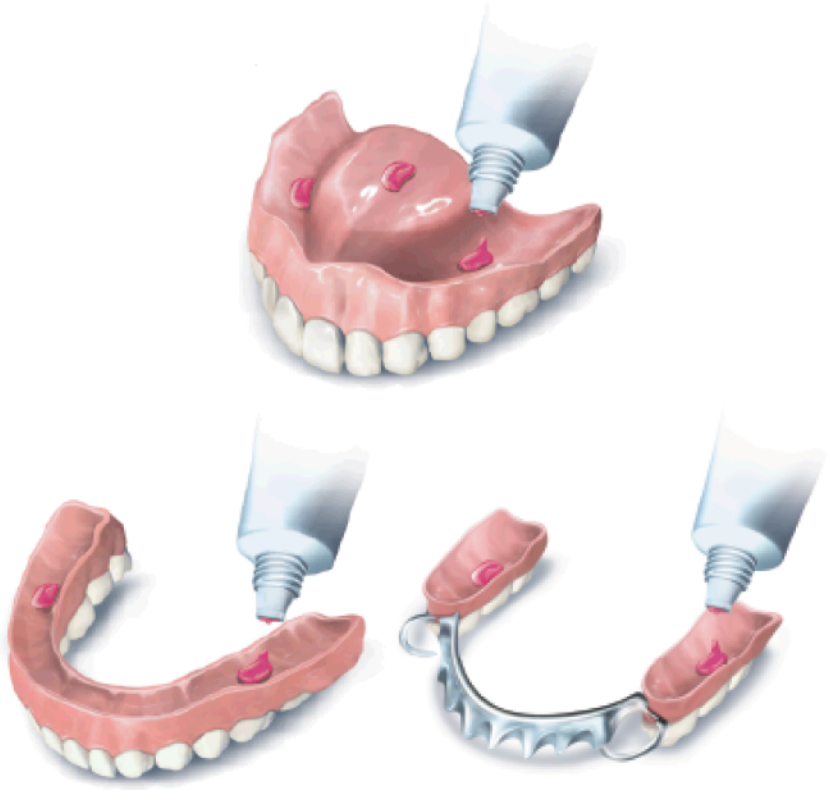
3. **Please describe below what you LIKED or DISLIKED about the denture adhesive.**

LIKED	

DISLIKED	

12.5. Appendix V – Denture Adhesive Application Instructions (Super Poligrip®)

Super Poligrip® (Reference Product)



APPLYING TO UPPER (AND WHERE NECESSARY LOWER) DENTURES:

1. Clean and dry dentures.
2. Pre-dispense sufficient denture adhesive to remove any potential separation in order to ensure product uniformity prior to application to the denture.
3. Apply product in strips, not too close to the denture edges (3 strips should be applied to the upper denture and 2 on the lower denture where necessary) as indicated in the images.
4. Maxillary dentures should be weighed before and after adhesive application to ensure correct dose applied (1±0.05 gram).

5. Where necessary, denture adhesive application to the lower denture should be sufficient to fully retain the lower denture in order to ensure accuracy of maxillary denture dislodgement bite force measures; please note that the lower denture images are for illustrative purposes only.
6. Have subjects rinse their mouth with water before inserting dentures.
7. Have subjects press dentures into place, hold firmly, and bite down for a few seconds to secure hold.

12.6. Appendix VI – Denture Adhesive Application Instructions (Experimental Denture Adhesives with a thin nozzle)

Experimental Denture Adhesives with Precision Applicator (Test Products)

APPLYING TO UPPER DENTURES:

1. Clean and dry upper dentures.
2. Pre-dispense sufficient denture adhesive to remove any potential separation in order to ensure product uniformity prior to application to the denture.
3. Apply product in long continuous strips as shown in the image, not too close to the denture edge (3 strips should be applied to the upper denture).
4. Maxillary dentures should be weighed before and after adhesive application to ensure correct dose applied (1±0.05 gram).
5. Have subjects rinse their mouth with water before inserting the upper denture
6. Have subjects press upper denture into place, hold firmly, and bite down for a few seconds to secure hold

SIGNATURE PAGE

Project CCI protocol

Date	Signed By
22-Feb-2017 06:26:52	PPD
Justification	Biostatistics Approval

Date	Signed By
22-Feb-2017 09:38:16	PPD
Justification	Approved

Date	Signed By
23-Feb-2017 07:00:52	PPD
Justification	Approved

Date	Signed By
23-Feb-2017 14:35:38	PPD
Justification	Clinical Operations Approval

Date	Signed By
Justification	

Date	Signed By
Justification	