CONFIDENTIAL

STATISTICAL ANALYSIS PLAN FOR PROTOCOL 206233

A Proof of Principle Bite Force Study Using Two New Test Adhesives and a Currently Marketed Denture Adhesive

BIOSTATISTICS DEPARTMENT

GLAXOSMITHKLINE CONSUMER HEALTHCARE

INVENTIV HEALTH CLINICAL

PPD

INDIA

PPD (Manager, Biostatistics)

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Glossary

AE	Adverse Event
ANCOVA	Analysis of Covariance
AOB	Area Over Baseline
AUC	Area Under the Curve
eCRF	Electronic Case Report Form
GSKCH	GlaxoSmithKline Consumer Healthcare
hr	hour
ITT	Intent To Treat
lbs	Libras (pounds)
MedDRA	Medical Dictionary for Regulatory Activities
Mins	Minutes
MFC	Manufacture Formulation Code
N/A	Not Applicable
OST	Oral Soft Tissue
PP	Per Protocol
PT	Preferred Term
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SOC	System Organ Class

1 Introduction

This document describes the statistical methods and data presentations to be used in the summary and analysis of the final data from Protocol 206233. This Statistical Analysis Plan (SAP) will be approved before unblinding and database freeze.

SAS version 9.4 will be used for the analyses. All statistical analyses mentioned in this SAP will be performed by inVentiv Health Clinical.

2 Objectives

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/	Scores from subject-completed questionnaires on product ooze, at 0.5

after-taste, texture and assess ease of removal	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 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 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.

3.1. 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 [redacted]	CCI [redacted]	CCI [redacted]	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

4 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 CCI. This was the larger SD among two similar earlier studies: CCI and CCI The delta of 2.01 was obtained from the study CCI. 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 CCI, CCI and CCI. 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 100,000 simulations.

5 Data Considerations

5.1 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. Listings of adverse events and incidents will be produced for the "All Subjects" population which includes all subjects that are identified and screened for entry into the study.

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.

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 is felt will affect the assessment of efficacy
- Weight of denture adhesive applied is outside the range 1±0.05 grams

The following will be included in the review of protocol violations but will be reviewed on a case-by-case basis to determine whether the data should be excluded from a PP analysis:

- Test day visits separated by less than 24 hours will be reviewed on a case-by-case basis prior to database lock to determine if any time points for any of the subjects will be excluded.
- Bite force measurements outside the time window of ±5 mins for the 0.5, 1, 3, 6, 9 and 12-hour assessments, will be reviewed on a case-by-case basis prior

to database lock to determine if any time points for any of the subjects will be excluded. For the ITT analysis, assessments will be assigned to the nominal visit, irrespective of whether the assessment took place within the time window or not.

Protocol violations which warrant exclusion from efficacy analysis will be identified between the statistician and clinical research director or designee, ahead of database freeze and breaking the study blind.

5.2 Subgroups/Stratification

There are no specific subgroups or strata which need to be considered.

5.3 Time Windows

Time windows for the test day visits and bite force assessments will be reviewed as mentioned above during the blinded data review. According to the protocol there will be at least 24 hours (up to 14 days) between treatment visits to allow recovery from the bite force procedures. Also according to the protocol 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.

6 Demographics and Baseline Characteristics

6.1 Subject Disposition

The subject disposition summary will include number of subjects screened, randomised, withdrawals (including reason), and the number of subjects in safety, ITT and PP populations. Subject disposition by study period will also be presented.

6.2 Demographics

Summary of demographic information will include age, gender, race and ethnicity. Categorical measures (gender, race and ethnicity) will be summarized by the number and percentage of subjects in each category. Descriptive statistics for age will include the mean, median, standard deviation and minimum/maximum.

6.3 Baseline Characteristics

Baseline bite force data will be summarised as part of the efficacy presentations. No additional baseline characteristics will be presented.

7 Treatment Compliance and Concomitant Medications

7.1 Treatment Compliance

The adhesive will be applied to dentures by one member of the study staff therefore excellent compliance is anticipated. Compliance will not be summarized; however, the instances where the weight of the adhesive used is outside the tolerance windows (1g ± 0.05 grams) will be listed for the blinded data review.

7.2 Concomitant Medications

Concomitant medication data will not be presented in the study report. A listing of concomitant medications will be produced for evaluation of protocol violators only.

8 Efficacy Analysis

The ITT population will be the primary population for the analyses of efficacy; a PP analysis 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.

For all parametric analyses, all assumptions 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).

8.1 Primary Efficacy Analysis

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 or the baseline 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.

8.2 Secondary Efficacy Analysis

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

From the ANCOVA model described above, treatment difference for each of the two test adhesives versus Super Poligrip® Free and with each other 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.

8.3 Exploratory/Other Efficacy Analysis

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

Other efficacy bite-force efficacy variables analysed will be bite force AOBs over 0.5, 1, 3, 6 and 9 hours respectively. Each of these 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 data from the questionnaires and the denture adhesive weights will be listed and tabulated using descriptive statistics.

9 Safety Analysis

The safety profile of the study treatments will be assessed with respect to adverse events (AEs) and incidents. Oral soft tissue (OST) abnormalities are included as AEs if they appear or worsen after the initial assessment.

All safety data will be reported for the Safety population as per actual treatment received. All subjects screened will be included in the list of AEs.

All AEs will be reviewed by the Clinical Research Director or Designee prior to database freeze and will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). During this review stage, AEs will be further categorized as oral or non-oral.

AEs will be regarded as treatment emergent if they occur on or after the date and time of the pre-treatment OST exam at the randomisation visit. All other AEs prior to this will be considered non-treatment emergent. AEs that occur during inter-test day washout are assigned to the last treatment received.

The following summary tables and listings will be presented by treatment group.

- Table of treatment emergent AEs by Oral/Non-Oral and Preferred Term
- Table of treatment emergent AEs by SOC and Preferred Term
- Table of Treatment emergent treatment related AEs by Oral/Non-Oral and Preferred Term
- Listing of all AEs (including Non-treatment emergent from All Subjects).
- Listing of serious AEs. (if there are none a null listing will be produced, if there are >5 treatment emergent SAEs a table will be produced by SOC and PT)
- Table of Non Serious treatment emergent AEs by SOC and Preferred Term. (only produced if there are > 5 SAEs)
- Listing of incidents (if there are none a null listing will be produced)

No inferential analyses will be performed to compare treatments with respect to safety.

10 Interim Analysis

No interim analysis is planned for this study.

11 Topline Summary

The following outputs will be produced for the topline report.

Datasets/Tables	Description
Datasets	STAT1, STAT2
Tables	Table 9.1.1 – Subject Disposition Table 9.1.3 – Protocol Violations Leading To Exclusion From Per Protocol Analysis – ITT Population Table 9.3.1 – Summary of Bite Force (lbs) by Time – ITT Population Table 9.3.2.1 – Summary of AOB by Time – ITT Population Table 9.3.2.2 – Summary of AOB (0-12 Hours) – PP Population Table 9.4.4 – Listing Of All Adverse Events – All Subjects

The following table will be produced in .rtf format for input into the topline report:

Table 1: Statistical Analysis of Between Treatment Group AOB over 12 hours (ITT Population)

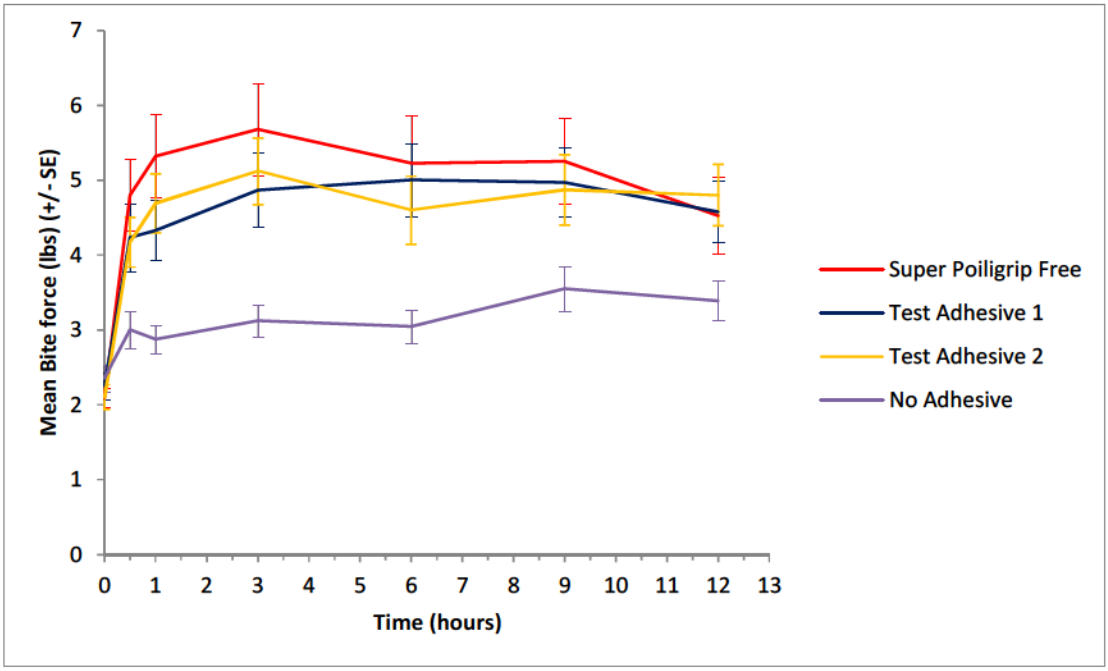
Parameter	Time Point	Treatment Comparison	Difference	Lower CI	Upper CI	P-value
AOB	0-12 hours	Super Poligrip Free vs. No Adhesive	x.xx	x.xx	x.xx	x.xxxx
		Test Adhesive 1 vs. No Adhesive	x.xx	x.xx	x.xx	x.xxxx
		Test Adhesive 2 vs. No Adhesive	x.xx	x.xx	x.xx	x.xxxx
		Test Adhesive 1 vs. Super Poligrip Free	x.xx	x.xx	x.xx	x.xxxx
		Test Adhesive 2 vs. Super Poligrip Free	x.xx	x.xx	x.xx	x.xxxx
		Test Adhesive 1 vs. Test Adhesive 2	x.xx	x.xx	x.xx	x.xxxx

Positive control adhesive: Super Poligrip Free Adhesive Cream (USA); Test Adhesive 1: CCI Test Adhesive 2: CCI No adhesive
[1] From ANCOVA with period and treatment as fixed effects, subject as random effect, and subject-level and period-level pre treatment baseline bite force (parameterized as period-level minus subject-level) as covariates.
[2] Difference is first-named treatment minus second-named treatment such that a positive difference favors the first named treatment.

A similar table titled "Table 2: Statistical Analysis of Between Treatment Group AOB over 12 hours (PP Population)" using the PP population will be produced in the .rtf format for the topline report if it is determined at the Blinded Data Review that a Per Protocol analysis will be performed.

The following figure will be produced in .rtf format for input into the topline report:

Figure 1: Bite force (lbs) value over time by treatment group (ITT Population)



12 Changes to Planned Analysis

The analyses for efficacy has been re-organised to match the primary, secondary and other objectives.

13 References

None.

Appendix 1 Study Schedule

SCHEDULE OF EVENTS

Procedure/ Assessment	Screening Visit 1		Treatment 1 Visit 2		Treatment 2 Visit 3		Treatment 3 Visit 4		Treatment 4 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			X[8]		X[8]		X[8]		X[8]

Between 1-14 days of screening

Between 1-14 days

Between 1-14 days

Between 1-14 days

staff to maxillary denture[8]								
Incisal Bite Force Measurements[9]			X[9]		X[9]		X[9]	X[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

Appendix 2 List of Tables, Figures & Listings

In all outputs, the treatment labels and order for presentation in tables and listings is as follows:

'Treatment 1' to be displayed as 'Test Adhesive 1'
'Treatment 2' to be displayed as 'Test Adhesive 2'
'Treatment 3' to be displayed as 'Super Poligrip Free'
'Treatment 4' to be displayed as 'No Adhesive'

All tables and listings which make use of the above treatment labels will, in addition, include the following footnotes:

Test Adhesive 1 - CCI
Test Adhesive 2 - CCI
Super Poligrip Free Adhesive Cream (USA marketplace)
No Adhesive

For the list of tables below, PP tables will only be produced if there is more than a 10% difference between the ITT and PP populations in any of the treatment groups.

TABLES

Table No.	Table Title (including population)	Standard	Template/ Comment
Table 9.1.1	Subject Disposition – All Screened Subjects		Appendix 3
Table 9.1.2	Subject Disposition by Sequence Group and Period – All Screened Subjects		Appendix 3
Table 9.1.3	Protocol Violations Leading To Exclusion From Per Protocol Analysis – Intent To Treat Population		Appendix 3
Table 9.1.4	Summary of Denture Adhesive Weights (grams) – Intent To Treat Population		Appendix 3
Table 9.2.1	Demographic Characteristics – Safety Population	X	
Table 9.2.2	Demographic Characteristics – Intent To Treat Population	X	
Table 9.2.3	*Demographic Characteristics – Per Protocol Population*	*X*	*Only produce if ≥10% diff between ITT and PP populations in one treatment group*
Table 9.3.1	Summary of Bite Force (lbs) by Time – Intent To Treat Population		Appendix 3

Table 9.3.2.1	Summary of AOB by Time – Intent To Treat Population		9.3.1.1
Table 9.3.2.2	*Summary of AOB (0-12 Hours) – Per Protocol Population*		*9.3.1.1; Only produce if ≥10% diff between ITT and PP populations in one treatment group; display results for only $AOB_{0\text{-}12}$.*
Table 9.3.3.1	Statistical Analysis of Bite Force AOB by time – Intent To Treat Population		Appendix 3
Table 9.3.3.2	*Statistical Analysis of Bite Force AOB (0-12 Hours) – Per Protocol Population*		*9.3.2.1. Only produce if ≥10% diff between ITT and PP populations for at least one treatment group; display results for only $AOB_{0\text{-}12}$.*
Table 9.3.4	Summary of Questionnaire Data – All Randomised Subjects		Appendix 3
Table 9.4.1	Treatment Emergent Adverse Events by Oral/Non-Oral and Preferred Term – Safety Population	X	
Table 9.4.2	Treatment Emergent Adverse Events by System Organ Class (SOC) and Preferred Term – Safety Population	X	
Table 9.4.3	Treatment Related Treatment Emergent Adverse Events by Oral/Non-Oral and Preferred Term – Safety Population	X	
Table 9.4.4	Listing of All Adverse Events – All Subjects	X	
Table 9.4.5	Listing of Serious Adverse Events – All Subjects	X	
Table 9.4.6[#]	Non-Serious Treatment Emergent Adverse Events by System Organ Class (SOC) and Preferred Term – Safety Population		9.4.2

Only produced if there are >5 SAEs.

FIGURES

Figure No.	Figure Title (including population)	Standard	Template
Figure 9.1	Subject Profiles of Bite Force (lbs) – Intent To Treat Population		Appendix 3
Figure 9.2	Bite force (lbs) value over time by treatment – Intent To Treat Population		Appendix 3

LISTINGS

Listing No.	Listing Title	Standard	Template
Listing 2.1	Randomisation Information – All Randomised Subjects	X	
Listing 2.2	Denture Removal Questionnaire, Question 3 (Please describe below what you liked or dislike about the denture adhesive) – All Randomised Subjects		Appendix 3
Listing 2.3	Incidents – All Subjects	X	

Appendix 3 Templates for Tables, Figures & Listing

Protocol: 206233 Program Run Date: ddmonyyyy

Table 9.1.1
Subject Disposition

	Treatment 1 N (%)	Treatment 2 N (%)	Treatment 3 N (%)	Treatment 4 N (%)	Overall N (%)
TOTAL SUBJECTS SCREENED					XX
SUBJECTS NOT RANDOMISED					XX
DID NOT MEET STUDY CRITERIA					XX (XX.XX)
ADVERSE EVENT					XX (XX.XX)
PROTOCOL DEVIATION					XX (XX.XX)
WITHDRAWAL OF CONSENT					XX (XX.XX)
OTHER					XX (XX.XX)
SUBJECTS RANDOMISED					XX
STARTED PERIOD 1	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
COMPLETED PERIOD 1	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
DID NOT COMPLETE PERIOD 1	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
ADVERSE EVENT	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
LOST TO FOLLOW - UP	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
PROTOCOL DEVIATION	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
WITHDRAWAL OF CONSENT	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
OTHER	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
...					
RECEIVED TREATMENT	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
COMPLETED TREATMENT/STUDY	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
DID NOT COMPLETE TREATMENT/STUDY	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
ADVERSE EVENT	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
LOST TO FOLLOW - UP	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
PROTOCOL DEVIATION	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
WITHDRAWAL OF CONSENT	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
OTHER	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
SAFETY POPULATION					XX
ITT POPULATION					XX
PP POPULATION					XX

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Program: PPD Source: Filename.xpt

Note to programmers: Percentages to be calculated from SUBJECTS NOT RANDOMISED (top section) and SUBJECTS RANDOMISED (remaining sections).

Protocol: 206233 Program Run Date: DDMMMYYYY

Table 9.1.2
Subject Disposition by Sequence Group and Period

Study Population: All Screened Subjects (N=XX)

	Overall N (%)	Sequence 1 N (%)	Sequence 2 N (%)	Sequence 3 N (%)	ETC. N (%)
TOTAL SUBJECTS SCREENED	XX				
SUBJECTS NOT RANDOMISED	XX				
DID NOT MEET STUDY CRITERIA	XX				
ADVERSE EVENT	XX				
ETC					
SUBJECTS RANDOMISED	XX	XX	XX	XX	XX
PERIOD 1:					
STARTED PERIOD	XX	XX	XX	XX	XX
COMPLETED	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
DID NOT COMPLETE	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
DID NOT MEET STUDY CRITERIA	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
ADVERSE EVENT	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
ETC					
WASHOUT PERIOD 1:					
STARTED PERIOD	XX	XX	XX	XX	XX
COMPLETED	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
DID NOT COMPLETE	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
DID NOT MEET STUDY CRITERIA	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
ADVERSE EVENT	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
ETC					
PERIOD 2:					
STARTED PERIOD	XX	XX	XX	XX	XX
COMPLETED	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
DID NOT COMPLETE	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
DID NOT MEET STUDY CRITERIA	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
ADVERSE EVENT	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
ETC					
WASHOUT PERIOD 2:					
STARTED PERIOD	XX	XX	XX	XX	XX

	Overall N (%)	Sequence 1 N (%)	Sequence 2 N (%)	Sequence 3 N (%)	ETC. N (%)
COMPLETED	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
DID NOT COMPLETE	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
DID NOT MEET STUDY CRITERIA	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
ADVERSE EVENT	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
ETC					
PERIOD 3:					
STARTED PERIOD	XX	XX	XX	XX	XX
COMPLETED	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
DID NOT COMPLETE	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
DID NOT MEET STUDY CRITERIA	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
ADVERSE EVENT	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
ETC					
...					
SAFETY POPULATION	XX	XX	XX	XX	XX
ITT POPULATION	XX	XX	XX	XX	XX
PP POPULATION	XX	XX	XX	XX	XX

Seq 1 = seq1, Seq 2 = seq2, Seq 3 = seq3, Seq 4 = seq4, Seq 5 = seq5, Seq 6 = seq6, Seq 7 = seq7 Seq 8 = seq8, Seq 9 = seq9, Seq 10 = seq10
A = xxxx, B = xxxx, C = xxxx, D = xxx.

Program: PPD Source: filename.xpt

Programming note: Percentages to be computed using number of subjects starting each period as the denominator.
Sequence and treatment codes are from PPD and are to be displayed as described above.
Washout period is defined per subject as the interval starting the date after the last dose of each treatment through the day before the date of the first dose of the next treatment in the sequence.

Protocol: 206233 Program Run Date: ddmonyyyy

Table 9.1.3
Protocol Violations Leading To Exclusion From Per Protocol Analysis
ITT Population

Study Population: ITT (N=xxx)

	Treatment 1 (N=xx)	Treatment 2 (N=xx)	Treatment 3 (N=xx)	Treatment 4 (N=xx)	Overall (N=xxx)
NUMBER OF SUBJECTS WITH AT LEAST ONE MAJOR PROTOCOL VIOLATION					XX (XX.X)
NUMBER OF SUBJECTS EXCLUDED FROM THE PER PROTOCOL POPULATION					XX (X.X)
MAJOR PROTOCOL VIOLATIONS FOR SUBJECTS EXCLUDED FROM THE PER PROTOCOL POPULATION:					
VIOLATION 1					XX (X.X)
VIOLATION 2					XX (X.X)
MAJOR PROTOCOL VIOLATIONS LEADING TO DATA EXCLUSION ONLY:					
VIOLATION 1	XX (X.X)	XX (X.X)	XX (X.X)	XX (X.X)	XX (X.X)
VIOLATION 2	XX (X.X)	XX (X.X)	XX (X.X)	XX (X.X)	XX (X.X)

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Subjects may have more than one violation.

Program:PPD Source: Filename.xpt

Protocol: 206233 Program Run Date: DDMONYYYY

Table 9.1.4
Summary of Denture Adhesive Weights (grams)
ITT Population

Study Population: ITT (N=XX)

	Treatment 1 (N=XX)	Treatment 2 (N=XX)	Treatment 3 (N=XX)
N	XX	XX	XX
MEAN	XX.XX	XX.XX	XX.XX
SD	XX.XXX	XX.XXX	XX.XXX
SE	XX.XXX	XX.XXX	XX.XXX
MEDIAN	XX.XX	XX.XX	XX.XX
MINIMUM	XX.X	XX.X	XX.X
MAXIMUM	XX.X	XX.X	XX.X

Program: PPD Source: XXXX.XPT

Protocol: 206233 Program Run Date: DDMONYYYY

Table 9.3.1
Summary of Bite Force (lbs) by Time
ITT Population

Study Population: ITT (N=XX)

	Treatment 1 (N=XX)	Treatment 2 (N=XX)	Treatment 3 (N=XX)	Treatment 4 (N=XX)
BASELINE				
N	XX	XX	XX	XX
MEAN	XX.XX	XX.XX	XX.XX	XX.XX
SD	XX.XXX	XX.XXX	XX.XXX	XX.XXX
SE	XX.XXX	XX.XXX	XX.XXX	XX.XXX
MEDIAN	XX.XX	XX.XX	XX.XX	XX.XX
MINIMUM	XX.X	XX.X	XX.X	XX.X
MAXIMUM	XX.X	XX.X	XX.X	XX.X
0.5 HOUR				
N	XX	XX	XX	XX
MEAN	XX.XX	XX.XX	XX.XX	XX.XX
SD	XX.XXX	XX.XXX	XX.XXX	XX.XXX
SE	XX.XXX	XX.XXX	XX.XXX	XX.XXX
MEDIAN	XX.XX	XX.XX	XX.XX	XX.XX
MINIMUM	XX.X	XX.X	XX.X	XX.X
MAXIMUM	XX.X	XX.X	XX.X	XX.X

Program: PPD Source: XXXX.XPT

Programming note: Repeat for 1, 3, 6, 9 and 12 HOURS.
This is the same shell for Table 9.3.2.1. In that table first summarise AOB (0-12 Hours) followed by AOB (0-0.5 Hour), AOB (0-1 Hour), AOB (0-3 Hours), AOB (0-6 Hours) and AOB (0-9 Hours).

Protocol: 206233 Program Run Date: DDMONYYYY

Table 9.3.3.1
Statistical Analysis of Bite Force AOB by Time
ITT Population

Study Population: ITT (N=XX)

	Treatment 1 (N=XX)	Treatment 2 (N=XX)	Treatment 3 (N=XX)	Treatment 4 (N=XX)
AOB 12 HOURS				
ADJUSTED MEAN (SE) [1]	XX.XX	XX.XX	XX.XX	XX.XX
95% CI [1]	(XX.XX,XX.XX)	(XX.XX,XX.XX)	(XX.XX,XX.XX)	(XX.XX,XX.XX)
P-VALUE [1]	X.XXXX	X.XXXX	X.XXXX	X.XXXX

TREATMENT COMPARISONS	DIFFERENCE (95% CI) [1,2]	P-VALUE [1]
SUPER POLIGRIP FREE vs. NO ADHESIVE	X.XX (X.XX, X.XX)	X.XXXX
TEST ADHESIVE 1 vs. NO ADHESIVE	X.XX (X.XX, X.XX)	X.XXXX
TEST ADHESIVE 2 vs. NO ADHESIVE	X.XX (X.XX, X.XX)	X.XXXX
TEST ADHESIVE 1 vs. SUPER POLIGRIP FREE	X.XX (X.XX, X.XX)	X.XXXX
TEST ADHESIVE 2 vs. SUPER POLIGRIP FREE	X.XX (X.XX, X.XX)	X.XXXX
TEST ADHESIVE 1 vs. TEST ADHESIVE 2	X.XX (X.XX, X.XX)	X.XXXX

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[1] From ANCOVA with factors for subject (random effect), period and treatment, and subject-level and period-level pre-treatment baseline bite force (parameterized as period-level minus subject-level) as covariates.
[2] Difference is first-named treatment minus second-named treatment such that a positive difference favours the first named treatment.

Program: PPD Source: XXXX.XPT

Programming note: Repeat for AOB 0.5, AOB 1, AOB 3, AOB 6 and AOB 9 HOURS.

Protocol: 206233

Program Run Date: DDMONYYYY

Table 9.3.4
Summary of Questionnaire Data
All Randomised Subjects

	Treatment 1 (N=XX)	Treatment 2 (N=XX)	Treatment 3 (N=XX)
Product Ooze Questionnaire (0.5 hour)			
Q1: How long after inserting your denture did you experience denture adhesive oozing out of your upper denture?			
Immediately	XX (XX.X)	XX (XX.X)	XX (XX.X)
Less than approximately 10 minutes	XX (XX.X)	XX (XX.X)	XX (XX.X)
Approximately 10 to 20 minutes	XX (XX.X)	XX (XX.X)	XX (XX.X)
Approximately 20 to 30 minutes	XX (XX.X)	XX (XX.X)	XX (XX.X)
No ooze experienced	XX (XX.X)	XX (XX.X)	XX (XX.X)
Sensory Questionnaire (12 hours)			
Q1: How would you rate your overall opinion of the denture adhesive?			
Dislike extremely	XX (XX.X)	XX (XX.X)	XX (XX.X)
Dislike moderately	XX (XX.X)	XX (XX.X)	XX (XX.X)
Dislike slightly	XX (XX.X)	XX (XX.X)	XX (XX.X)
Neither like nor dislike	XX (XX.X)	XX (XX.X)	XX (XX.X)
Like slightly	XX (XX.X)	XX (XX.X)	XX (XX.X)
Like moderately	XX (XX.X)	XX (XX.X)	XX (XX.X)
Like extremely	XX (XX.X)	XX (XX.X)	XX (XX.X)
...			
Denture Removal Questionnaire (12 hours)			
Q1: How easy was it to remove the denture from the mouth?			
Not at all easy	XX (XX.X)	XX (XX.X)	XX (XX.X)
...			

Program: PPD

Source: XXXX.XPT

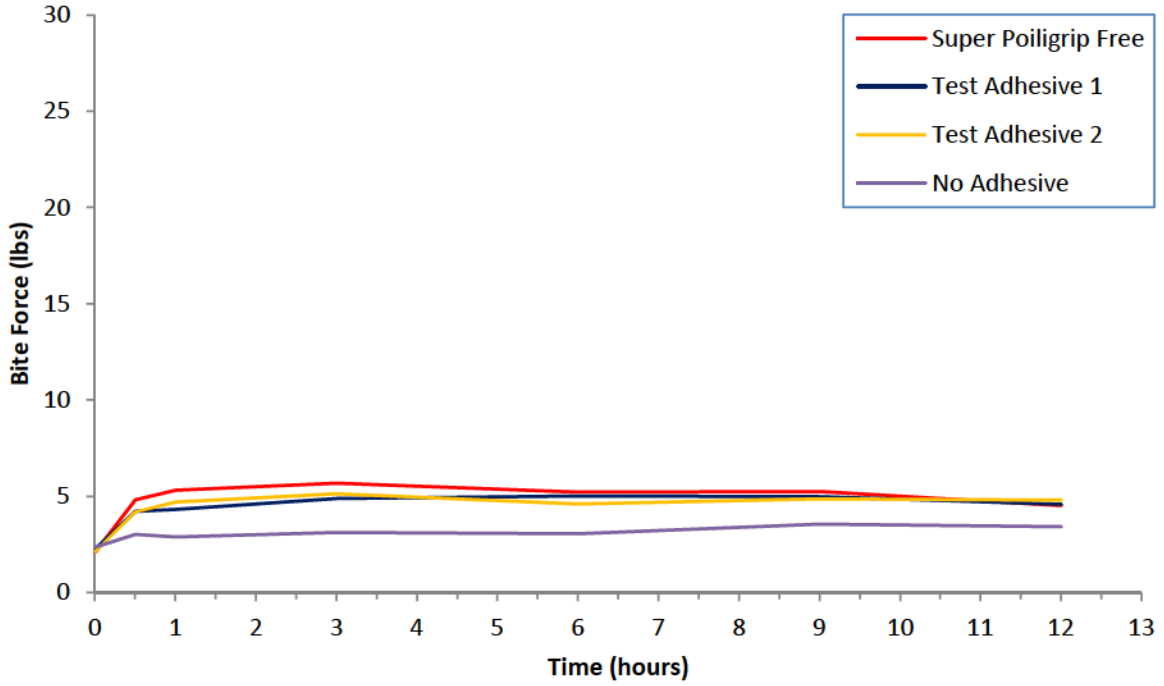
Protocol: 206233

Program Run Date: DDMONYYYY

Figure 9.1
Subject Profiles of Bite Force (lbs)
ITT Population

Study Population: ITT (N=XX)

Subject = 01S000x



Program:PPD

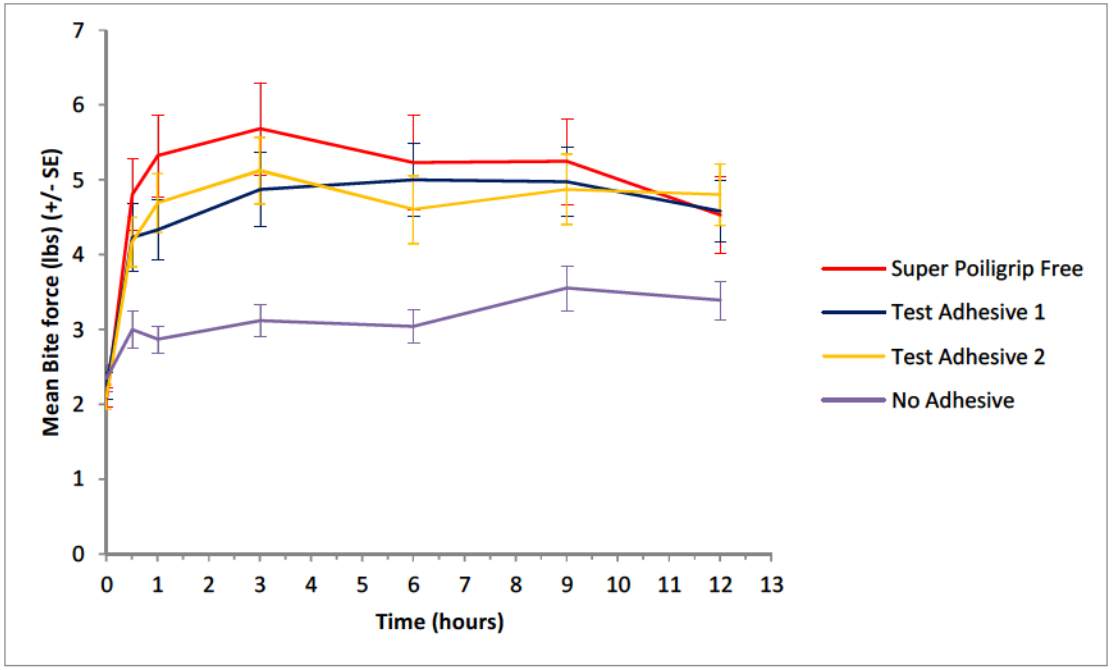
Source: XXXX.XPT

Protocol: 206233

Program Run Date: DDMONYYYY

Figure 9.2
Bite force (lbs) value over time by treatment
ITT Population

Study Population: ITT (N=XX)



Program:PPD

Source: XXXX.XPT

Protocol: 206233 Program Run Date: DDMONYYYY

Data Listing 2.2
Denture Removal Questionnaire, Question 3 (Please describe below what you liked or dislike about the denture adhesive)
All Randomised Subjects

Subject Number	Liked/ Disliked	Response
01S0001	Liked	xxxxxxxxxxxx
	Disliked	xxxxxxxxxxxx
01S0002	Liked	xxxxxxxxxxxx
	Disliked	xxxxxxxxxxxx

Program: PPD Source: XXXXX.XPT

SIGNATURE PAGE

Statistical Analysis Plan for Study 206233.docx

Date	Signed By
27-Mar-2017 03:25:53	PPD
Justification	Biostatistics Approval

Date	Signed By
27-Mar-2017 09:54:12	PPD
Justification	Approved

Date	Signed By
Justification	

Date	Signed By
Justification	

Date	Signed By
Justification	

Date	Signed By
Justification	