CONFIDENTIAL

STATISTICAL ANALYSIS PLAN FOR PROTOCOL 204930

Study to Investigate the Impact on Oral Health Related Quality of Life of Managing Dentine Hypersensitivity by a Daily Use Anti-Sensitivity Toothpaste

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Glossary

AE	Adverse Event
AM	Ante Meridiem (Morning)
ANCOVA	Analysis of Covariance
CI	Confidence Interval
cm	Centimetre
CRO	Clinical Research Organisation
DH	Dentine hypersensitivity
DHEQ	Dentine Hypersensitivity Evaluation Questionnaire
eCRF	electronic Case Report Form
EAR	Erosion, Abrasion, Recession
g	Grams
GI	Gingival Index
GSKCH	GlaxoSmithKline Consumer Healthcare
ITT	Intention-to-Treat
LMS	Labelled Magnitude Scale
mm	Millimetre
MGI	Modified Gingival Index
OST	Oral Soft Tissue
PP	Per Protocol
ppm	Parts Per Million
SAP	Statistical Analysis Plan
TPI	Turesky Modification of the Quigley-Hein Plaque Index
UK	United Kingdom
VAS	Visual Analogue Scale
w/w	Weight/Weight Ratio

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 204930. The statistical analysis plan (SAP) will be finalised and approved prior to database lock. This is a non comparative study.

2 Objectives

Primary	
To monitor the impact of long term management of DH over a 24 week period, with twice daily use of a sensitivity toothpaste, on the oral health related quality of life in sensitivity sufferers, as measured by the DHEQ.	Change from baseline in DHEQ endpoints over time.
Exploratory	
To evaluate changes in dentine hypersensitivity over the 24 week treatment period, including the number of sensitive teeth, as measured by Schiff Sensitivity Score to assess examiner performance on this measure.	Mean Schiff Sensitivity Score for all timepoints. Change from baseline in Schiff sensitivity score (two test teeth) for all timepoints. Change from baseline in Schiff sensitivity score (all qualifying teeth) for all timepoints.
To evaluate changes in dentine hypersensitivity over the 24 week treatment period, as measured by Labelled Magnitude Scales (LMS).	At each time point the mean LMS (of each of 4 VAS scales) and change from baseline (for the two test teeth) and will be calculated.

3 Study Design

Overall Design
This multi-site, non-comparative design study will be used to monitor the impact of long term management of DH with daily use of a sensitivity toothpaste on the quality of life of a population of sensitivity sufferers. Changes in oral health related quality of life will be monitored using the DHEQ. The study will be conducted in subjects in good general health, with pre-existing self-reported and clinically diagnosed tooth sensitivity at screening.
Visit 1 - Screening Visit

The following assessments will be conducted in the order written:

- Written informed consent.
- Review of the oral care products the subject is currently using to confirm they do not contain any ingredients intended for treating sensitive teeth.
- Demographics, concomitant medications and medical history.
- Oral examination including an oral soft tissue (OST) examination and oral hard tissue (OHT) assessments to determine eligible teeth.
- Qualifying evaporative air sensitivity.
- Inclusion/exclusion criteria review.
- Confirmation of subject eligibility.
- Dispensation of acclimatisation toothpaste, toothbrush, diary and timer.
- Supervised brushing with acclimatisation toothpaste.
- Adverse Events (AEs) will be documented from completion of the supervised brushing with acclimatisation toothpaste.

Visit 2 - Baseline Visit (Day 0)

The following assessments will be conducted in the order written:

- Review of concomitant medications and AEs.
- Return of acclimatisation toothpaste, toothbrush and diary.
- Review of completed diary to determine usage compliance.
- Inclusion/exclusion criteria review.
- Confirmation of subject eligibility and continuance.
- Completion of DHEQ Section 1 and Section 2.
- LMS Training Exercise
- OST and OHT examinations.
- Evaporative air sensitivity assessment (Schiff Sensitivity Scale, LMS) on all eligible teeth from Visit 1.
- Selection of two test teeth.
- Dispensation of study toothpaste, toothbrush and diary.
- Supervised brushing with study treatment.
- AEs and Incidents from supervised brushing with study treatment

Visit 3 - Week 4 (Day 28 ± 3)
Visit 4 – Week 8 (Day 56 ± 3)
Visit 5 – Week 12 (Day 84 ± 3)
Visit 6 – Week 16 (Day 112 ± 3)
Visit 7 – Week 20 (Day 140 ± 3)

The following assessments will be conducted in the order written:

- Review of concomitant medications, AEs and incidents.
- Return of study toothpaste and diary. New toothbrush at Week 12.
- Review of completed diary to determine usage compliance.

• Inclusion/exclusion criteria review. • Confirmation of subject continuance. • Completion of DHEQ Section 1 (Q7-9) & Section 2. • OST and OHT examinations. • Evaporative air sensitivity assessment (Schiff Sensitivity Scale, LMS) on two test teeth. • Evaporative air sensitivity assessment (Schiff Sensitivity Scale) on remaining eligible teeth from Visit 1. • Dispensation of study toothpaste and diary (and toothbrush at Visit 5). • Supervised brushing with study treatment. • AEs and Incidents from supervised brushing with study treatment
Visit 8 – Week 24 (Day 168 ± 3)
The following assessments will be conducted in the order written: • Review of concomitant medications, AEs and incidents. • Return of study toothpaste, toothbrush and diary. • Review of completed diary to determine usage compliance. • Confirmation of subject continuance. • Completion of DHEQ Section 1 (Q7-9) & Section 2. • OST and OHT examination. • Evaporative air sensitivity assessment (Schiff Sensitivity Scale, LMS) on two selected test teeth. • Evaporative air sensitivity assessment (Schiff Sensitivity Scale) on remaining eligible teeth from Visit 1. • AEs and incidents will be recorded for 5 days after last treatment.

The study product is:

- Dentifrice containing 0.454% w/w stannous fluoride (1100ppm fluoride) Sensodyne Repair and Protect Daily Repair Toothpaste. German marketplace

4 Sample Size Determination

The sample size is based on DHEQ total Score, restrictions, adaptation, social impact, emotional impact and identity, from a previous study [GSKCH Study RH01897]. A sample size of 60 subjects will have at least 90% power to detect significant changes to week 24 for each of the DHEQ variables, with a significance level (alpha) of 0.05 using a two-sided one-sample t-test. No adjustments for multiple testing have been used. Approximately 75 eligible subjects will be allocated the study toothpaste in order to ensure that approximately 60 subjects complete the study. Sixty subjects

will provide reasonable precision on estimates of DHEQ response and clinical DH assessments.

5 Data Considerations

5.1 Analysis Populations

The Safety population will consist of all subjects who received the study toothpaste.

The intention to treat (ITT) population will be defined as all subjects who received the study toothpaste and have at least one post- baseline clinical assessment.

The per-protocol (PP) population will be defined as all subjects who received the study toothpaste and have at least one post-baseline clinical assessment and have no protocol violations deemed to affect clinical assessments during the study.

The following will be considered a protocol violation which may warrant exclusion from the PP analysis:

- Violation of inclusion or exclusion criteria that are deemed to affect efficacy.
- Medical history which is deemed to affect efficacy.
- Use of a medication before or during the study, which is felt to affect the assessment of efficacy. The time points affected will be determined prior to database lock.
- Not receiving any study treatment.

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:

- Non compliance with assigned treatment regimen. Treatment compliance will be reviewed on a case-by-case basis prior to database lock to determine the time points from which subject data will be excluded. More details will be given in the Blinded Review Specification Document.
- Assessments outside the time window of the designated time windows Visit 3 - Week 4 (Day 28 ± 3), Visit 4 – Week 8 (Day 56 ± 3), Visit 5 – Week 12 (Day 84 ± 3), Visit 6 – Week 16 (Day 112 ± 3), Visit 7 – Week 20 (Day 140 ± 3) and Week 24 (Day 168 ± 3) will be reviewed on a case-by-case basis prior

to database lock to determine the time points from which subject data will be excluded. For the analysis, assessments will be assigned to the nominal visit, irrespective of whether the assessment took place within the visit window.

Protocol violations which warrant exclusion from efficacy analysis will be identified between the statistician and Clinical Research Director or designee, before database lock. Further details will be provided in the Data Review Specifications document.

Analysis of all quality of life or hypersensitivity endpoints will be performed on the ITT population. Analysis on the PP population will also be performed if there is more than 10% difference in the number of subjects for the ITT and PP populations.

5.2 Subgroups/Stratification

No subgroup or stratified analyses are planned.

5.3 Criteria for Evaluation

DHEQ measures captured in the study will be used evaluate changes in oral health related in quality of life over time. OST abnormalities, incidents and AEs reported in the study will be used for safety evaluations of the study treatments.

5.3.1 Criteria for Assessing Efficacy

There are no formal success criteria in this study however it is expected that statistically significant changes from baseline will be observed for the DHEQ measures, in particular the Total score.

5.3.2 Criteria for Assessing Tolerability

Safety will be assessed with respect to AEs, Incidents and OST abnormalities (oral tolerability).

6 Demographics and Baseline Characteristics

6.1 Subject Disposition

The subject disposition summary will include the number of screened subjects and screen failures overall. The number and percentage of subjects, in the Safety, ITT and PP populations will be presented. The percentages will be based upon the total number of subjects in the Safety population.

The number and percentage of subjects completing the study and not completing the study, including a breakdown of the reasons for not completing the study, will be presented. The percentages are based upon the total number of subjects in the Safety population.

A separate summary table of protocol violations leading to exclusion from PP analyses will be produced indicating the number and percentage of subjects with each violation. Percentages will be based on the ITT population.

6.2 Demographics and Baseline Characteristics

Descriptive statistics (number of subjects, mean, standard deviation, median, minimum and maximum for continuous variables, and frequency and percentage for categorical variables) will be provided for demographic on baseline data on the Safety, ITT and PP populations.

7 Treatment Compliance and Concomitant Medications

7.1 Treatment Compliance

Diaries will be used throughout the study to a) allow the subject to familiarize themselves with their completion during the acclimatisation phase and b) promote compliance during the treatment phase. Subjects will not be withdrawn from the study due to missed brushings but will be reminded to use the products supplied as per the instructions provided and to complete the diary after each product usage to encourage compliance.

Study site staff will review the diaries at the start of each visit for compliance and any reports of changes/new medications.

To ensure that subjects understand the dose of toothpaste to be used, staff will demonstrate what is meant by a 'full ribbon' (i.e. covering the length of the toothbrush head), and brushing will be supervised at all assessment visits (at the end of the visit procedures).

Subjects will receive a product use diary. This will outline the brushing instructions and will be used to record each brushing occasion during the study. Subjects will be provided with a new diary at screening, baseline, Week 4, Week 8, Week 12, Week 16 and Week 20 which they will return to the site at the subsequent visit. The number of missed or extra brushings will be recorded in the eCRF and may lead to exclusion from the PP population.

Subjects will also be asked to bring all tubes of toothpaste to each study visit for a visual compliance check of product usage.

7.2 Concomitant Medications

Concomitant medications used during the study will be databased but no formal listing of these data will be produced. These data will be reviewed for potential exclusions from the PP population.

7.3 Medical History

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. Any concomitant therapy taken in the 30 days prior to the Screening Visit and throughout the study will also be recorded.

8 Efficacy Analysis

8.1 Primary Analysis

The null hypothesis for the primary analysis will be:

H_0= There is no difference from baseline in DHEQ endpoints over time.

The alternative hypothesis will be:

H_1= There is statistically significance difference from baseline in DHEQ endpoints over time.

The following DHEQ endpoints will be analysed:

- Section 1, questions 7, 8 and 9 as separate questions
- Total Score (34 item total from Section 2 questions 1 to 34)
- Domains:
  1. Restrictions (4 item total from Section 2 questions 1 to 4)
  2. Adaptation (12 item total from Section 2 questions 5 to 16)
  3. Social Impact (5 item total from Section 2 questions 17 to 21)
  4. Emotional Impact (8 item total from Section 2 questions 22 to 29)
  5. Identity (5 item total from Section 2 questions 30 to 34)
- Global Oral Health Rating (response to Section 2 question 35)
- Effect on Life Overall (4 item total from Section 2 questions 36 to 39)

Above DHEQ endpoints will be analysed using mixed effect ANOVA with Visit and site as fixed effect, subject as random effect. Adjusted Means will be computed for each visit. Using this model, the post baseline visit will be compared to the baseline visit and difference of their effect will be computed along with P-values and 95% confidence interval.

The visit by site interaction will be investigated by including the visit by site interaction term. If the visit by site interaction term is not significant at the 10% level of significance then this term will be removed from the model.

If the visit site interaction term is significant at 10% level of significance then the interaction will be included in the model and all model estimates (Adjusted Means, 95% CIs and P-values) for within and between visits will be reported separately for each site and based on results from visit by site interaction.

Each of the DHEQ endpoints will be summarised by time point (Baseline, Week 4, 8, 12, 16, 20 and 24).

Standard summary measures, 95% CIs and p- values will be presented. A plot of means of raw scores over time (mean ± standard errors) will also be presented for all measures.

Due to the exploratory nature of the study no correction of multiple testing will be performed.

Summary statistics (N, Percentage) will be provided for section 1 (Q1-Q6) and section 2 (Q1 - Q39) of DHEQ questionnaire.

The assumption of normality and homogeneity of variance in the ANOVA model will be investigated. Violation of these assumptions may be overcome using suitable transformation or performing a non-parametric test (e.g., the Wilcoxon signed-rank test).

8.2 Exploratory Analyses

The following exploratory analyses will be conducted.

At each time point the mean Schiff Sensitivity Score (for the two test teeth and all qualifying teeth) and mean LMS scores [each of 4 scales (description, tolerability, description, intensity] as well as the change from baseline will be calculated.

The above each endpoint will be analysed using mixed effect ANOVA with visit and site as fixed effect, subject as random effect. Adjusted Means will be computed for each visit. Using this model, the post baseline visit will be compared to the baseline visit and difference of their effect will be computed along with P-values and 95% confidence interval.

The visit by site interaction will be investigated by including the visit by site interaction term. If the visit by site interaction term is not significant at the 10% level of significance then this term will be removed from the model.

If the visit site interaction term is significant at 10% level of significance then the interaction will be included in the model and all model estimates (Adjusted Means, 95% CIs and P-values) for within and between visits will be reported separately for each site and based on results from visit by site interaction.

Standard summary measures, 95% CIs and p-values will be presented. A plot of means of raw scores over time (mean ± standard errors) will also be presented for all measures.

The assumption of normality and homogeneity of variance in the ANOVA model will be investigated. Violation of these assumptions may be overcome using suitable transformation or performing a non-parametric test (e.g., the Wilcoxon signed-rank test).

The percentage of teeth that are sensitive (Schiff sensitivity score >0 of all qualifying teeth from screening (termed 'the qualifying teeth') will be summarised for each timepoint and also plotted over time.

9 Safety Analysis

The safety profile of the study dentifrice will be assessed with respect to adverse events (AEs). 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 start date and time of the first treatment application. All other AEs prior to this will be considered non-treatment emergent.

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)
- Listing of incidents (if there are none a null listing will be produced)
- Table of Non Serious treatment emergent AEs by SOC and Preferred Term. (only produced if there are > 5 SAEs)

10 Interim Analysis

No interim analysis is planned for this study.

11 Topline Summary Tables

The following tables and figures will be provided for top-line report.

Table No./ Datasets	Title
Table 9.1.1	Subject Disposition All Screened Subjects
Table 9.3.1.1	Summary and Statistical Analysis of Dentine Hypersensitivity Experience Questionnaire [DHEQ Section 1] Intent to Treat Population
Table 9.3.1.2	Summary and Statistical Analysis of Dentine Hypersensitivity Experience Questionnaire [DHEQ Section 2 -All Domains] Intent to Treat Population
Table 9.4.1	Treatment Emergent Adverse Events by Oral/non-Oral and preferred term Safety Population
Table 9.4.3	Treatment Emergent Treatment Related Adverse Events by Oral/non-Oral and preferred term Safety Population
Table 9.4.5	Listing of all AEs (including Non-treatment emergent from All Subjects).
Datasets*	ADSL.sas7bdt, ADAE.sas7bdt, ADDHEQ.sas7bdt STAT1_TOP.sas7bdt and STAT2_TOP.sas7bdt
Figure No.	**Title**
Figure 9.1.2.1	DHEQ Total Score over Time Intent to Treat Population
Figure 9.1.3.1	DHEQ Domains over Time Intent to Treat Population (Note Restrictions, Social Impact, Identity, Adaptation, Emotional Impact)

* Validated datasets will be sufficient for the topline report.

Appendix 1 Study Schedule

Procedure	Screening Visit 1		Baseline Visit 2 Week 0 (Day 0)	Visit 3 Week 4 (Day 28 ±3)	Visit 4 Week 8 (Day 56 ±3)	Visit 5 Week 12 (Day 84 ±3)	Visit 6 Week 16 (Day 112 ±3)	Visit 7 Week 20 (Day 140 ±3)	Visit 8 Week 24 (Day 168 ±3)
Informed Consent	X	Acclimatisation Period - Minimum 3 weeks – Maximum 6 weeks							
Demographics, Medical History	X								
Current/Concomitant Medications	X		X	X	X	X	X	X	X
Inclusion/Exclusion	X		X						
Subject Eligibility	X		X						
Subject Continuance			X	X	X	X	X	X	X
Oral Soft Tissue (OST) and Oral Hard Tissue (OHT) Assessment	X		X	X	X	X	X	X	X
Eligible Teeth Assessments (Dentition Exclusions, EAR, MGI, Tooth Mobility)	X								
Qualifying Evaporative Air Sensitivity (Y/N)	X								
Dispense Acclimatisation Toothpaste, Toothbrush, Diary and Timer	X								
Supervised Brushing with Acclimatisation Toothpaste	X								
Return Acclimatisation Toothpaste, Toothbrush and Diary			X						
DHEQ completion [1,5]			X	X	X	X	X	X	X
LMS[5] training			X						
Evaporative Air Assessment (Schiff Sensitivity Score, LMS[5]) *on all Eligible Teeth from Screening*		Acclimatisation Period	X						
Selection of 2 *'Test Teeth'*			X						
Evaporative Air Assessment (Schiff Sensitivity Score, LMS[5]) *on 2 'Test Teeth'*				X	X	X	X	X	X

Procedure	Screening Visit 1		Baseline Visit 2 Week 0 (Day 0)	Visit 3 Week 4 (Day 28 ±3)	Visit 4 Week 8 (Day 56 ±3)	Visit 5 Week 12 (Day 84 ±3)	Visit 6 Week 16 (Day 112 ±3)	Visit 7 Week 20 (Day 140 ±3)	Visit 8 Week 24 (Day 168 ±3)
Evaporative Air Assessment (Schiff Sensitivity Score) *on Remaining Eligible Teeth from Screening*				X	X	X	X	X	X
Dispense Study Product			X[2]	X	X	X[2]	X	X	
Supervised Brushing			X	X[3]	X[3]	X[3]	X[3]	X[3]	
Return Study Product and Diary				X	X	X	X	X	X
Compliance checks			X	X	X	X	X	X	X
Adverse Events	X[4]		X	X	X	X	X	X	X
Incidents			X	X	X	X	X	X	X
Study Conclusion									X

1. To be completed prior to OST examination and any clinical assessments
2. Dispense a new toothbrush at this visit also
3. Subject instructed to bring all supplies back to all subsequent visits
4. After first supervised brushing with acclimatisation product
5. To be completed by subjects

Appendix 2 List of Tables, Figures & Listings

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Table 9.1.1	Subject Disposition All Screened Subjects	Standard
Table 9.2.1.1	Demographic Characteristics Safety Population	Appendix3
Table 9.2.1.2	Demographic Characteristics Intent to Treat Population	Table 9.2.1.1
Table 9.2.1.3	Table 9.2.1.2 on PP as required.	Table 9.2.1.1
Table 9.3.1.1	Summary Statistics of Individual Dental Hypersensitivity Experience Questionnaire (DHEQ) Questions (Section 1, Question 1 to 6) by Site and Overall — ITT Population	Appendix3
Table 9.3.1.2	Summary Statistics of Individual Dental Hypersensitivity Experience Questionnaire (DHEQ) Questions (Section 2, Question 1 to 39) by Site and Overall — ITT Population	Table 9.3.1.1
Table 9.3.1.3	Summary and Statistical Analysis of Dentine Hypersensitivity Experience Questionnaire [DHEQ Section 1, Question 7 to 9] Intent to Treat Population	Appendix3
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Table 9.3.1.5/6	9.3.1.3/4 on PP as required.	
Table 9.3.2.1	Summary Statistics of Evaporative (Air) Sensitivity (Schiff Sensitivity Score) By Site and Overall Intent to Treat Population	Appendix3
Table 9.3.2.2	Summary and Statistical Analysis of Measures of Dentinal Hypersensitivity (Schiff Sensitivity Score) Over Time Intent to treat Population	Appendix3

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Table 9.3.3.1	Summary of Measures of Dentinal Hypersensitivity (LMS) by Site and Overall Intent to treat Population	Table 9.3.2.1
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Table 9.3.4.1	Summary of Percentage Qualifying Teeth Over Time Intent to treat Population	Appendix3
Table 9.4.1	Treatment Emergent Adverse Events by Oral/non-Oral and preferred term Safety Population	Standard
Table 9.4.2	Treatment emergent AEs by SOC and Preferred Term Safety Population	Standard
Table 9.4.3	Treatment Emergent Treatment Related Adverse Events by Oral/non-Oral and preferred term Safety Population	Standard
Table 9.4.4	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)	Standard
Table 9.4.5	Listing of all AEs (including Non-treatment emergent from All Subjects).	Standard
Table 9.4.6	Table of Non Serious treatment emergent AEs by SOC and Preferred Term. (only produced if there are > 5 SAEs)	Standard
Listing 2.1	Listing of Oral Soft Tissue Abnormalities	Standard
Listing 2.2	Listing of Incidents	Standard
Listing 2.3	Listing of Randomisation Details	Standard
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Figure 9.1.1	DHEQ Section 1 Question 7/8/9 –Over Time Intent to Treat Population	Appendix 3
Figure 9.1.2	DHEQ Section 1 Question 7/8/9 Over Time by Site- Intent to Treat Population	Figure 9.1.1
Figure 9.2.1	DHEQ Total Score over Time Intent to Treat Population	Figure 9.1.1
Figure 9.2.2	DHEQ Total Score over Time by Site Intent to Treat Population	Figure 9.1.1

Table No.	Title	Specification
Figure 9.3.1	DHEQ Domains over Time Intent to Treat Population (Note Restrictions, Social Impact, Identity, Adaptation, Emotional Impact)	Figure 9.1.1
Figure 9.3.2	DHEQ Domains over Time by Site Intent to Treat Population (Note Restrictions, Social Impact, Identity, Adaptation, Emotional Impact)	Figure 9.1.1
Figure 9.4.1	DHEQ Global Health rating and Effect on Life Over Time Intent to Treat Population	Figure 9.1.1
Figure 9.4.2	DHEQ Global Health rating and Effect on Life over Time by Site Intent to Treat Population	Figure 9.1.1
Figure 9.5.1	DHEQ Effect on Life Overall Life Over Time Intent to Treat Population	Figure 9.1.1
Figure 9.5.2	DHEQ Effect on Life Overall Life Over Time by Site Intent to Treat Population	Figure 9.1.1
Figure 9.6.1	Schiff Sensitivity Score Over Time Intent to Treat Population	Appendix3
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Figure 9.7.1	% Qualifying Teeth Sensitive (Schiff Sensitivity Score >0) Over Time Intent to Treat Population	Appendix3
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Figure 9.8.1	Labelled Magnitude Scales (Mean Two Test Teeth) Over Time Intent to Treat Population	Appendix 3
Figure 9.8.2	Labelled Magnitude Scales (Mean Two Test Teeth) Over Time by Site Intent to Treat Population	Figure 9.8.1

Appendix3 Templates for Tables, Figures & Listings

DHEQ

11 Measures are summarized from this questionnaire.

Section 1 Q7: Intensity of Sensations (VAS 0-10cm), Section 1 Q8: How Bothersome are Sensations (VAS 0-10cm), Section 1 Q9: Ability to Tolerate Sensations (VAS 0-10cm), Total Score (34 item total from Section 2 questions 1 to 34), Restrictions (4 item total from Section 2 questions 1 to 4), Adaptation (12 item total from Section 2 questions 5 to 16), Social Impact (5 item total from Section 2 questions 17 to 21), Emotional Impact (8 item total from Section 2 questions 22 to 29), Identity (5 item total from Section 2 questions 30 to 34), Global Oral Health Rating (response to Section 2 question 35), Effect on Life Overall (4 item total from Section 2 questions 36 to 39)

Please add footnote reference to the Study Product at the end of each output:
Dentifrice containing 0.454% w/w stannous fluoride (1100ppm fluoride) Sensodyne Repair and Protect Daily Repair Toothpaste CCI

CCI

Protocol: 204930

Program Run Date: DDMMMYYYY

Table 9.2.1.1
Demographic Characteristics
Safety Population

Study Population: Safety (N=xxx)

	SITE 1 (N=XX)	SITE 2 (N=XX)	Overall (N=XX)
SEX N (%)			
MALE	XX (XX.X)	XX (XX.X)	XX (XX.X)
FEMALE	XX (XX.X)	XX (XX.X)	XX (XX.X)
RACE N (%)			
AFRICAN AMERICAN/AFRICAN HERITAGE	XX (XX.X)	XX (XX.X)	XX (XX.X)
AMERICAN INDIAN OR ALASKAN NATIVE	XX (XX.X)	XX (XX.X)	XX (XX.X)
ASIAN - CENTRAL/SOUTH ASIAN HERITAGE	XX (XX.X)	XX (XX.X)	XX (XX.X)
ASIAN - EAST ASIAN HERITAGE	XX (XX.X)	XX (XX.X)	XX (XX.X)
ASIAN - SOUTH EAST ASIAN HERITAGE	XX (XX.X)	XX (XX.X)	XX (XX.X)
NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	XX (XX.X)	XX (XX.X)	XX (XX.X)
WHITE - ARABIC/NORTH AFRICAN HERITAGE	XX (XX.X)	XX (XX.X)	XX (XX.X)
WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE	XX (XX.X)	XX (XX.X)	XX (XX.X)
ETHNICITY N (%)			
HISPANIC OR LATINO	XX (XX.X)	XX (XX.X)	XX (XX.X)
NOT HISPANIC OR LATINO	XX (XX.X)	XX (XX.X)	XX (XX.X)
AGE (YEARS)			
N	XX	XX	XX
MEAN	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX
MEDIAN	XX.X	XX.X	XX.X
MINIMUM	XX	XX	XX
MAXIMUM	XX	XX	XX

Protocol: 204930 Program Run Date: DDMMMYYYY

Table 9.3.1.1
Summary of Individual Dental Hypersensitivity Experience Questionnaire (DHEQ) Questions
[DHEQ Section 1, Question 1 to 6] By Site and Overall

Study Population: ITT (N=XX)

	SITE 1 (N=XX)	SITE 2 (N=XX)	OVERALL (N=XX)
Q 1: WHICH OF THE FOLLOWING BEST DESCRIBES ANY SENSATIONS YOU MAY HAVE FELT IN YOUR TEETH? N (%)			
BASELINE			
ITCHY	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
ACHING	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
SHOOTING	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
PIERCING	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
...	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
MISSING	XX	XX	XX
Q 2: HOW LONG HAVE YOU BEEN EXPERIENCING ANY SENSATIONS IN YOUR TEETH? N (%)			
BASELINE			
LESS THAN 6 MONTHS (1)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
MORE THAN SIX MONTHS BUT LESS THAN A YEAR (2)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
MORE THAN A YEAR BUT LESS THAN FIVE YEARS (3)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
MORE THAN FIVE YEARS BUT LESS THAN 20 YEARS (4)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
MORE THAN 20 YEARS (5)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
NONE (0)	XX (XX.X%)	XX (XX.X%)	XX (XX.X%)
MISSING	XX	XX	XX

PPD PPD

Programming Note: 1) XX.X % = XX/N *100 i.e. N is number of subjects. 2) Please populate same summary for the remaining questions.

Protocol: 204930 Program Run Date: DDMMMYYYY

Table 9.3.1.3

Summary and Statistical Analysis of Dentine Hypersensitivity Experience Questionnaire

[DHEQ Section 1, Question 7 to 10]

Study Population: ITT (N=XX)

Q7. ON THE SCALE OF 1 TO 10 HOW INTENSE ARE THE SENSATIONS?							
			WEEK 4			WEEK 8	
	BASELINE	BASELINE [1]	VALUES	CFB	BASELINE [1]	VALUES	CFB
N	XX	XX	XX	XX	XX	XX	XX
MISSING	XX	XX	XX	XX	XX	XX	XX
MEAN	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
SE	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
MEDIAN	X.X	X.X	X.X	X.X	X.X	X.X	X.X
MINIMUM	XX	XX	XX	XX	XX	XX	XX
MAXIMUM	XX	XX	XX	XX	XX	XX	XX
ADJUSTED MEAN [2]			XX.XX			XX.XX	
95 % CIS [2]			[X.XX, X.XX]			[X.XX, X.XX]	
P-VALUES [2]			0.XXXX			0.XXXX	

WEEK COMPARISON	DIFFERENCE [2,3]	95% CIS [2]	P-VALUES [2]
WEEK 0 VS. WEEK 4	XX.XX	[X.XX, X.XX]	0.XXXX
WEEK 0 VS. WEEK 8	XX.XX	[X.XX, X.XX]	0.XXXX

[1] Baseline only includes those subjects who have a corresponding post-baseline assessment. Baseline = Day 0.
[2] From mixed effect ANOVA model with visit and site as fixed effect, subject as random effect.
[2] Difference is first named week minus second named week such that a positive difference favors the first named week.
CFB= Change From Baseline;

PPD PPD

Programming note: Same tables will populated for- 'Week 12','Week 16 ', 'Week 20' and 'Week 24'. Please repeat tables for the Q8 and Q9.

Protocol: 207238 Program Run Date: DDMMMYYYY

Table 9.3.2.1
Summary Statistics of Evaporative (Air) Sensitivity (Schiff Sensitivity Score) By Site and Overall
Intent to Treat Population

Study Population: Intent to Treat Population (N=XXX)

TWO TEST TEETH	SITE 1 (N=XX)	SITE 2 (N=XX)	OVERALL (N=XX)
BASELINE			
N (NON-MISSING)			
MEAN	XXX	XXX	XXX
SD	X.XXX	X.XXX	X.XXX
SE	X.XXX	X.XXX	X.XXX
MEDIAN	XX.X	XX.X	XX.X
MINIMUM	XX.X	XX.X	XX.X
MAXIMUM	XX.X	XX.X	XX.X
WEEK 4			
N (NON-MISSING)	XXX	XXX	XXX
MEAN	X.XXX	X.XXX	X.XXX
SD	X.XXX	X.XXX	X.XXX
SE	XX.X	XX.X	XX.X
MEDIAN	XX.X	XX.X	XX.X
MINIMUM	XX.X	XX.X	XX.X
MAXIMUM			
WEEK 8....			

PPD PPD

Programmer note: Please repeat same table for all qualifying teeth.

Protocol: 204930 Program Run Date: DDMMMYYYY

Table 9.3.2.2

Summary and Statistical Analysis of Measures of Dentinal Hypersensitivity (Schiff Sensitivity Score) Over Time

Study Population: ITT (N=XX)

TWO TEST TEETH

	BASELINE	BASELINE [1]	WEEK 4 VALUES	CFB [1]	BASELINE [1]	WEEK 8 VALUES	CFB [1]
N	XX	XX	XX	XX	XX	XX	XX
MISSING	XX	XX	XX	XX	XX	XX	XX
MEAN	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
SE	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
MEDIAN	X.X	X.X	X.X	X.X	X.X	X.X	X.X
MINIMUM	XX	XX	XX	XX	XX	XX	XX
MAXIMUM	XX	XX	XX	XX	XX	XX	XX
ADJUSTED MEAN [2]			XX.XX			XX.XX	
95 % CIS [2]			[X.XX, X.XX]			[X.XX, X.XX]	
P-VALUES [2]			0.XXXX			0.XXXX	

WEEK COMPARISON	DIFFERENCE [2,3]	95% CIS [2]	P-VALUES [2]
WEEK 0 VS. WEEK 4	XX.XX	[X.XX, X.XX]	0.XXXX
WEEK 0 VS. WEEK 8	XX.XX	[X.XX, X.XX]	0.XXXX

[1] Baseline only includes those subjects who have a corresponding post-baseline assessment. Baseline = Day 0.
[2] From mixed effect ANOVA model with visit and site as fixed effect, subject as random effect.
[2] Difference is first named week minus second named week such that a positive difference favors the first named week.
CFB= Change From Baseline;

PPD PPD

Programming note: The same table will populated for- 'Week 12''Week 16 ', 'Week 20' and 'Week 24'. Please repeat the same summary for Qualifying Teeth.

Protocol: 204930 Program Run Date: DDMMMYYYY

Table 9.3.4.1

Summary of % Qualifying Teeth Sensitive over Time

Study Population: ITT (N=XX)

% OF QUALIFYING TEETH SENSITIVE	BASELINE	WEEK 4	WEEK 8	WEEK 12	WEEK 16	WEEK 20	WEEK 24
N	XX	XX	XX	XX	XX	XX	XX
MEAN	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
SE	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
MEDIAN	X.X	X.X	X.X	X.X	X.X	X.X	X.X
MINIMUM	XX	XX	XX	XX	XX	XX	XX
MAXIMUM	XX	XX	XX	XX	XX	XX	XX
PROPORTION OF QUALIFYING TEETH SENSITIVE	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX

Footnote: % Qualifying Teeth Sensitive will be calculating follows:

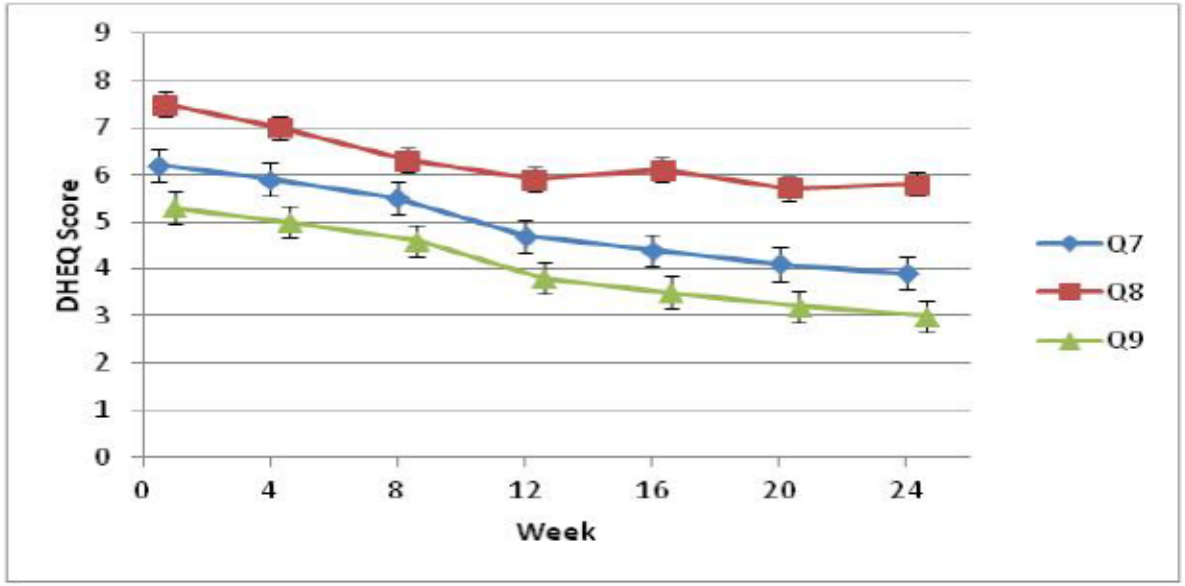
Percentage Qualifying Teeth sensitive = (Schiff sensitivity score >0 for qualifying teeth /All qualifying teeth from screening)*100

PPD PPD

Protocol: 204930

Program Run Date: DDMMMYYYY

Figure 9.1
DHEQ Section 1 Question 7/8/9 –Over Time
Intent to Treat Population



Values are mean ± SE

Q7: On a scale of 1-10 how intense are the sensations?
Q8: On a scale of 1-10 how bothered are you by any sensations?
Q9: On a scale of 1-10 how well can you tolerate sensations?

Protocol: 204930

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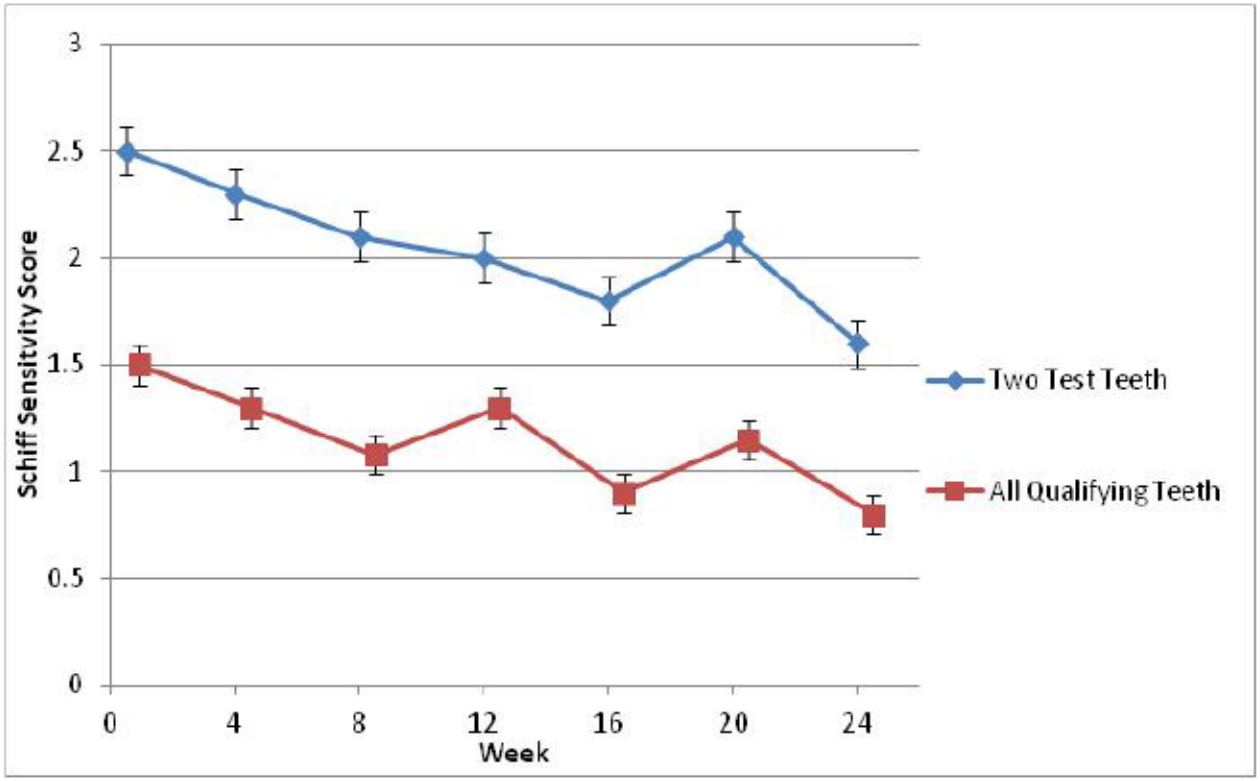
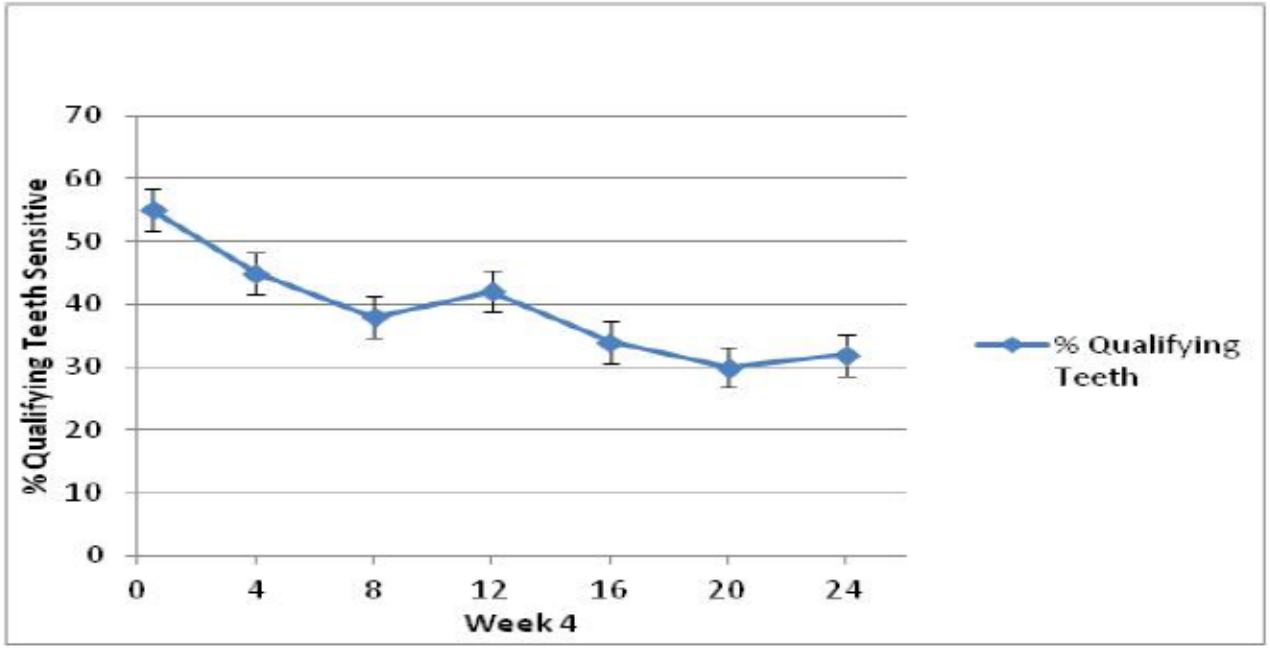
Figure 9.6.1
Schiff Sensitivity Score over Time
Intent to Treat Population



Protocol: 204930

Program Run Date: DDMMMYYYY

Figure 9.7.1
% Qualifying Teeth Sensitive over Time
Intent to Treat Population



Percentage Qualifying Teeth sensitive = (Schiff sensitivity score >0 for qualifying teeth /All qualifying teeth from screening)*100

Protocol: 204930

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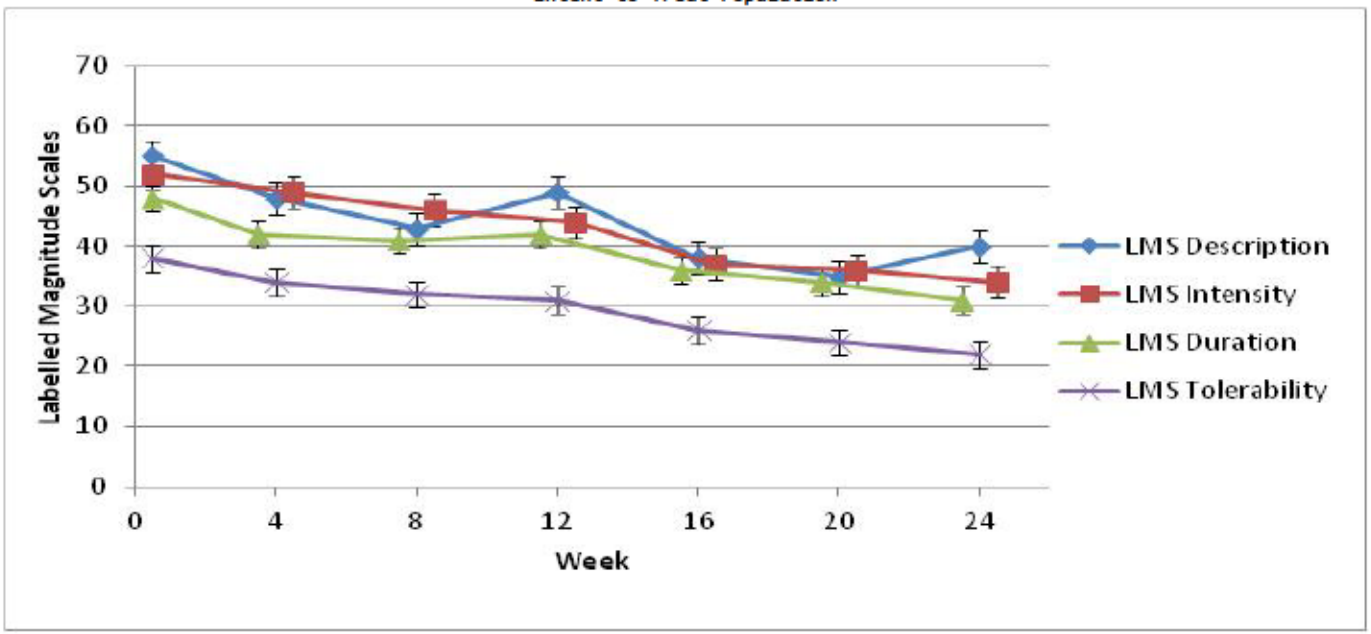
Figure 9.8.1
Labelled Magnitude Scales over Time
Intent to Treat Population



LMS range 0-100mm

SIGNATURE PAGE

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Date	Signed By
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Justification	Approved

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10-Nov-2016 09:05:41	PPD
Justification	Biostatistics Approval

Date	Signed By
Justification	

Date	Signed By
Justification	

Date	Signed By
Justification	

Date	Signed By
Justification	