Statistical Analysis Plan for Protocol

207196

A Randomized, Parallel-group, Evaluator-blind, No-treatment and Positive-controlled, Single-site, Proof-of-concept Clinical Study to Evaluate the Cosmetic Benefit Provided by 8 Weeks of Twice-daily Topical Application of a Developmental Moisturizing Cream with Niacinamide in Healthy Subjects with Sensitive, Oily, Blemish-prone Skin

NCT03093181

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GlaxoSmithKline
Consumer Healthcare

STATISTICAL REPORTING AND ANALYSIS PLAN

A randomised, parallel-group, evaluator-blind, no-treatment and positive controlled, single-site, proof of concept clinical study to evaluate the cosmetic benefit provided by 8 weeks of twice-daily topical application of a developmental moisturising cream with niacinamide in healthy subjects with sensitive, oily, blemish-prone skin

Protocol Number: 207196

Phase: NA

Document History

Document	Version Date	Summary of Changes (New analysis or Change in planned analysis)
Original Analysis Plan	19-Sept-2017	Not applicable (N/A)

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Glossary

AE	Adverse Event
ANCOVA	Analysis of covariance
BDRM	Blind Data Review Meeting
CI	Confidence Interval
ITT	Intent-to-Treat
MedDRA	Medical Dictionary for Regulatory Activities
PP	Per Protocol
RAP	Statistical Reporting and Analysis Plan
RH	Relative Humidity
RLR	Review Listing Requirement
SOC	System Organ Class
TEAE	Treatment Emergent Adverse Event

The purpose of this Statistical Reporting and Analysis Plan is to describe the planned analyses and outputs to be included in the Clinical Study Report for Protocol 207196.

1 Summary of Key Protocol Information

This randomised, parallel-group, evaluator-blind, no-treatment and positive controlled, single-site, proof of concept clinical study is designed to evaluate the cosmetic benefit provided by 8 weeks of twice-daily topical application of a developmental moisturising cream with niacinamide in healthy subjects with sensitive, oily, blemish-prone skin.

General safety and tolerability will be assessed based on the frequency and severity of Adverse Events (AEs).

1.1 Study Design

This randomised, parallel-group, evaluator-blind, no-treatment and positive controlled, single-site, proof of concept clinical study follows the study schedule below.

Procedure/Assessment	Visit 1 Day-7 to -5	Visit 2 Day 1	Visit 3 Day 8 ± 1	Visit 4 Day 29 ± 2	Visit 5 Day 57 ± 2
	Screening /Washout	Baseline	1 Week of Application	4 Week of Application	8 Week of Application
Inform Consent	✓				
Demographics	✓				
Medical History	✓				
Current / Concomitant Medication	✓	✓	✓	✓	✓
Adverse Events		✓	✓	✓	✓
Diary Review (Compliance)[1]		✓	✓	✓	✓
Continued Eligibility		✓	✓	✓	✓
Fitzpatrick Skin Type Assessment	✓				
Evaluator Assessment of Blemish Counts[2]	✓	✓4	✓	✓	✓
Forehead Sebumeter Measurement[3]	✓	✓4	✓	✓	✓
Inclusion / Exclusion Criteria	✓	✓5			
Subject Eligibility	✓	✓			
Washout Cleanser and Diary Dispensing	✓				
Randomisation		✓			

Corneometer Measurements[3]		✓4	✓	✓	✓
Image Capture		✓4			✓
Washout Cleanser return and Products Dispensing		✓			
Sebumeter Kinetic Measurements[3,9]		✓	✓	✓	✓
Supervised Product Application[6]		✓	✓	✓	
Acute Corneometer Measurements		✓7			
Products and Diary Return					✓
Subject Discharge from Study					✓
Lay Person Assessment of Overall Appearance of Blemishes (Photographs)[5]					✓

1. Evaluators must be blinded to diary review.

2. Blind evaluator assessment of papules and pustules, to be counted separately for the face, chin and cheeks.

3. Time Subjects must also acclimatize for a minimum of 30 minutes in a temperature (20 ± 1 degrees Celsius (ºC)) and humidity (50 ± 10% Relative Humidity (RH)) controlled room prior to any instrumental measurement being taken.

4. Baseline measurements (prior to any product application).

5. Only the inclusion and exclusion criteria in Appendix 2 will be reviewed at this visit.

6. Subjects randomised to positive control regimen will apply the positive control cleanser and positive control cream. Subjects randomised to the test product regimen will apply the standard cleanser and test product. Subjects randomised to the no treatment regimen will apply the standard cleanser only. Test product application will be overseen by a member of the study team who must not be involved in any clinical or instrumental assessment which could influence the study outcome.

7. Acute Corneometer assessments will be taken 1 hour ± 15 MINUTES, 3 hours ± 15 MINUTES and 8 hours ± 15 MINUTES after application of the cream for subjects randomised to the test product and positive control regimens and after cleansing for subjects randomised to the untreated regimen.

8. Lay person assessment of overall appearance of blemishes (Photographs) will take place after the completion of the clinical study.

9. Sebumeter kinetic measurements will be taken 5 ± 1 minutes and 90 ± 5 minutes after forehead cleansing.

1.2 Study Objectives

Objectives	Endpoints
Primary	
Evaluation of skin moisturisation (change from baseline) compared to no treatment	Corneometer values at 8 hours on Day 1
Secondary	
Evaluation of skin moisturisation (change from baseline) compared to no treatment	Corneometer values at 1 hour on Day 1, 3 hours on Day 1, 1 week, 4 weeks and 8 weeks
Evaluation of the overall appearance	Lay person assessment of the appearance

Objectives	Endpoints
of blemishes (change from baseline) compared to no treatment	of blemishes by photographic assessment at 8 weeks Evaluator assessment blemish count (sum of papules and pustules at forehead, chin and cheeks) at 1, 4 and 8 weeks Evaluator assessment of individual blemish count (individual count of papules and pustules at the forehead, chin and cheeks) at 1, 4 and 8 weeks
Evaluation of skin oiliness improvement (change from baseline) compared to no treatment	Sebumeter values at 1, 4 and 8 weeks Sebum excretion rate at 1, 4 and 8 weeks
To evaluate the safety of the test product	Frequency and severity of adverse events

1.3 Treatments

	Washout/ Standard Cleanser	Test Product	Positive Control Cleanser	Positive Control Moisturiser
Product Name	Simple Kind to Skin Moisturising Facial Wash	Moisturising Cream with Niacinamide	Neutrogena Visibly Clear Spot Clearing Facial Wash	Vivatinell Acnecinamide Gel Cream
Product Formulation Code (MFC)	Commercially Available (UK)	CCI	Commercially Available (UK)	Commercially Available (Turkey)
Application Quantity	Approx. 0.6 g	Approx. 0.6 g	Approx. 0.6 g	Approx. 0.6 g
Application Instructions	Use twice daily (morning and night) with at least 8 hours between product applications.	Use twice daily (morning and night) with at least 8 hours between product	Use twice daily (morning and night) with at least 8 hours between product applications.	Use twice daily (morning and night) with at least 8 hours between product applications.

	Washout/ Standard Cleanser	Test Product	Positive Control Cleanser	Positive Control Moisturiser
	Wet your face and hands with water. Dispense the product into your hands and apply to the face. Massage gently. Rinse with water and pat dry. Avoid contact with eyes. If contact occurs, rinse thoroughly with water.	applications. Dispense two pumps of product onto your fingertips and apply to your whole face, covering all blemishes. Avoid contact with eyes. If contact occurs, rinse thoroughly with water.	Wet your face and hands with water. Dispense the product into your hands and apply to the face. Massage gently. Rinse with water and pat dry. Avoid contact with eyes. If contact occurs, rinse thoroughly with water.	Apply a peasized quantity to your whole face, covering all blemishes. Avoid contact with eyes. If contact occurs, rinse thoroughly with water.

1.4 Sample Size Calculation

Approximately 200 female subjects aged 18-45 with self-assessed sensitive skin and a minimum of 8 and a maximum of 25 facial blemishes (papules and pustules, excluding the nose) will be screened to randomise 132 healthy subjects, to ensure approximately 40 subjects in the test product regimen, 40 subjects in the no treatment regimen and 40 subjects in the positive control regimen complete the study (Assuming a 10% dropout rate). Randomisation will be stratified by age (<21 years old, ≥21 years of age).

The sample size was based on clinical considerations. In a previous study of a cosmetic product, counts of papules and pustules decreased from a baseline mean of 27.6 to a mean of 13.5 at Week 8 (ref. Shalita 1995 IJD). With 40 subjects in both the test product and no-treatment regimens, a difference between groups at least 60% the magnitude of the standard deviation (assumed equal for both groups) would be detectable at two-sided alpha=0.05 with approximately 80% power.

2 Planned Analyses

2.1 Interim Analysis

No interim analysis is planned.

2.2 Final Analyses

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

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

3 Considerations for data analyses and Data Handling Conventions

3.1 Baseline Definition

For all endpoints the baseline value will be the latest before test product or positive control product for subjects randomised to the test regimen and positive control regimen, and before baseline cleansing for subjects randomised to the untreated regimen.

3.2 Subgroups/Stratifications

Eligible subjects will be stratified by age (<21 years, ≥21 years) when randomised into treatments. There are therefore two strata in this study:

- Stratum1: Subjects of age<21 years ;
- Stratum2: Subjects of age ≥21 years.

3.3 Timepoints and Visit Windows

Deviations from the scheduled assessment times should be avoided or kept to a minimum as possible. Any deviation will be noted in the blinded data review before database lock and subjects may be considered for exclusion from the per protocol population.

The following are the assessment time windows.

Visit	Time window
Visit 2	5-7 days after Visit 1. Visit 2 is baseline and counted as Day 1.
Visit 3	Day 8 ± 1 Day

Visit	Time window
Visit 4	Day 29 ± 2 Days
Visit 5	Day 57 ± 2 Days

Acute corneometer assessments will be taken 1 hour ± 15 MINUTES, 3 hours ± 15 MINUTES and 8 hours ± 15 MINUTES after application of the cream for subjects randomised to the test product and positive control regimens and after cleansing for subjects randomised to the untreated regimen.

Sebumeter kinetic measurements will be taken 5 ± 1 minutes and 90 ± 5 minutes after forehead cleansing.

4 Data Analysis

Data analysis will be performed by inVentiv Health Clinical. Prior to database closure a Blind Data Review Meeting (BDRM) will be conducted in which various aspects of the trial will be discussed and agreed. The statistical analysis software used will be SAS version 9.4.

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

4.1 Populations for Analysis

Tables described in this section will be produced for all randomised subjects, unless otherwise specified.

4.1.1 Subject Disposition

Screen failures will be defined as subjects who consent to participate in the study but are never subsequently randomised. A summary will be provided of the number of subjects screened and the number of screen failures.

Subject disposition will be summarised as the number and percentage of subjects (out of the number of randomised subjects) who complete the study, with the number who discontinue broken down by reason for discontinuation (Table 14.1.1). The table will also summarise the number and percent of subjects assigned to each analysis population (defined in Section 2.1.3). The summary will be presented by treatment and overall.

Subject disposition will be listed for randomised subjects (Listing 16.2.1.1) and non-randomised subjects (Listing 16.2.1.2) separately.

4.1.2 Protocol Deviations

Protocol deviations will be tracked by the study team throughout the conduct of the study. All deviations will be reviewed prior to unblinding and closure of the database to ensure all important violations are captured and categorised.

Major deviations identified as liable to influence the efficacy outcome will include follows:

- Deviation from the inclusion/exclusion criteria
- Use of prohibited medication
- Not receiving randomised treatment

Further deviations liable to influence the efficacy outcome will be given in the "Review Listing Requirement (RLR)" document and major deviations will be identified in blinded data review stage. The number and percentage of subjects with any major protocol deviations and with each type of major protocol deviations will be presented by treatment (Table 14.1.2) and listed (Listing 16.2.2.1). Any minor protocol deviations will be listed similarly (Listing 16.2.2.2).

4.1.3 Analysis Populations

Six analysis populations are defined.

Population	Definition / Criteria	Analyses Evaluated
All Screened Subjects	All subjects those who are screened	Disposition
Randomised	All subjects who are randomised and may or may not receive the application of the study products.	Protocol deviations
Safety	Safety population includes all subjects who are randomised and receive at least one dose of study product. For the no-treatment regimen, this will include any use of the cleanser post-randomisation.	Safety analysis
Intent-to-Treat (ITT)	The 'Intent to treat' (ITT) population includes all subjects who are in safety population and have at least one post baseline efficacy assessment.	Efficacy analysis
Per-Protocol (PP)	The Per Protocol (PP) population will consist of the subset of ITT subjects which excludes those subjects with major protocol deviations.	Efficacy analyses for corneometry and blemish count will also be performed on the PP population

The numbers of subjects included in each of the analysis populations, and the number excluded from each population broken down by the reason for exclusion will be presented (Table 14.1.3). Subjects excluded from any of the analysis populations will be listed (Listing 16.2.3.1).

4.2 Subject Demographics and Other Baseline Characteristics

4.2.1 Demographic Characteristics

Categorical demographic variables include sex, race and Fitzpatrick type. These variables will be summarised by the number and percentage of subjects with each relevant characteristic (Table 14.1.4.1 for the Safety population, Table 14.1.4.2 for the ITT population and Table 14.1.4.3 for the PP population). Age will be summarised by the mean, standard deviation (SD), median, minimum and maximum values. Baseline stratification will also be summarised by the number and percentage of subjects in each stratum. All summaries will be presented by treatment, and overall. All demographic information will be listed (Listing 16.2.4.1).

4.2.2 General Medical History

Medical history data will be listed in Listing 16.2.4.2 with start date and end date or ongoing at the start of study drug. A data listing will also be produced for evaluation of protocol violations at the blinded data review stage.

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

4.3.1 Study Product Compliance and Exposure

Study product compliance (using study products twice daily) will be listed (Listing 16.2.5.1) and checked at the blinded data review stage for evaluation of protocol violations. A compliance summary table will be provided for ITT population (Table 14.2.1).

4.3.2 Prior and Concomitant Medication

Prior and concomitant medication/non-drug treatments data will be listed (Listing 16.2.5.2, 16.2.5.3). Prior medications are defined as those stopped before the baseline administration of the study products. Concomitant medications are defined as those ongoing or started on or after the baseline administration of the study products.

A data listing will also be produced for evaluation of protocol violations at the blinded data review stage.

4.4 Analysis of Efficacy

Statistical testing of all endpoints in this study will be conducted at unadjusted two-sided significance level of 0.05. The null and alternative hypotheses are

- H_0: there is no difference between treatment groups;
- H_a: there is a difference between treatment groups.

While for this proof of concept study statistical significance ($p<0.05$) may not be achieved, these results will drive sample size projections for future studies. Due to the exploratory nature of the study, no adjustment to the alpha level for multiple comparisons will be made. P-values resulting from inferential testing will be considered primarily as summary statistics.

No statistical comparisons between the positive control regimen and the test product regimen are planned. The positive control is included to provide internal validation to the trial and to provide a reference point for estimates of effect size.

4.4.1 Primary Efficacy Endpoint

4.4.1.1 Primary Efficacy Endpoint Definition

The corneometer measurement of each subject at each assessment point will be calculated as the mean of the three repeated measurements of the subject at that assessment point.

The primary endpoint is the change from baseline in Corneometer measurement at 8 hours following the first product application. Data for the endpoint will be summarized by age stratum and treatment regimen (Table 14.2.2.2, 14.2.2.3 for the ITT population and Table 14.2.2.5, 14.2.2.6 for the PP population).

4.4.1.2 Statistical Hypothesis, Model, and Method of Analysis

Analysis of covariance (ANCOVA) will be applied with treatment as main effect, age stratification and baseline measurement as covariate. Least squares means and differences between least squares means for (i) test product and no treatment regimen; (ii) positive control and no treatment regimen will be presented, together with 95% confidence intervals (Table 14.2.2.1 for the ITT population, Table 14.2.2.4 for the PP population).

In the randomisation stage of the study, a substantial number of subjects were randomised using wrong age stratum randomisation scheme. In all summary and analyses involving age stratum, subjects will be assigned to correct age strata using their actual ages.

4.4.1.3 Supportive Analyses

The normality assumption for ANCOVA in primary analysis will be checked. If violated, non-parametric method such as Wilcoxon rank sum test may be applied.

4.4.2 Secondary Efficacy Variables

Secondary efficacy variables of the study are listed below.

4.4.2.1 Corneometer measurements at other time points

The change from baseline in Corneometer measurements at 1 and 3 hours following the first product application as well as at Weeks 1, 4 and 8 are secondary variables which will be summarized by age strata, treatment regimen and study visit (Table 14.2.2.2, 14.2.2.3 for the ITT population and Table 14.2.1.5, 14.2.1.6 for the PP population).

4.4.2.2 Sebumeter and sebum excretion rate

The sebumeter measurement of each subject at each visit will be calculated as the mean of the three repeated assessments of the subject at that visit. The sebum excretion rate of each subject at each visit will be calculated as the difference of sebumeter kinetic measurement 90 mins post forehead cleansing to 5 mins post forehead cleansing. The sebumetry and sebum excretion rate changes from baseline at Weeks 1, 4 and 8 are secondary variables which will be summarized by age strata, treatment regimen and study visit (Table 14.2.3.2, 14.2.3.3 for sebumeter and Table 14.2.4.2, 14.2.4.3 for sebum excretion rate, ITT population).

4.4.2.3 Blemish counts

Clinical assessment of blemish counts (papules and pustules) change from baseline at Weeks 1, 4 and 8 are secondary variables which will be summarized by age stratum, treatment regimen and study visit (Table 14.2.5.2, 14.2.5.3 for the ITT population and Table 14.2.5.5, 14.2.5.6 for the PP population).

4.4.2.4 Lay person assessment

The lay person assessment resulting from the ranking of blemish images (Week 8 image vs. Baseline image with judgement either 'Week 8 is better' or 'Baseline is better') is a secondary variable. The assessment will be performed using polarised images and non-polarised images separately by 24 raters. Summary statistics will be provided by treatment (Table 14.2.6.2, for polarized image, Table 14.2.7.2 for non-polarised image, ITT population).

4.4.3 Handling of Missing Values/Censoring/Discontinuations

Missing data will not be replaced or imputed. Dropouts will be included in analyses up to the point of discontinuation.

4.5 Analysis of Secondary Objectives

4.5.1 Efficacy

The change from baseline in corneometer measurements at 1 and 3 hours following the first product application as well as at Weeks 1, 4 and 8 will be analysed at each post-baseline time point using the same ANCOVA model as in primary analysis. Differences between least squares means for (i) test product and no treatment regimen; (ii) positive control and no treatment regimen will be presented, together with 95% confidence intervals. The normality assumption for ANCOVA will be checked. If violated, non-parametric method such as Wilcoxon rank sum test may be applied.

The sebumeter and sebumeter excretion rate changes from baseline at Weeks 1, 4 and 8 will be analysed at each post-baseline visit using ANCOVA with treatment main effect, age stratum (<21, ≥21 years of age) and baseline count as covariate. Differences between least squares means for (i) test product and no treatment regimen; (ii) positive control and no treatment regimen will be presented, together with 95% confidence intervals (Table 14.2.3.1 for sebumeter, Table 14.2.4.1 for sebumeter excretion rate). The normality assumption for ANCOVA will be checked. If violated, non-parametric method such as Wilcoxon rank sum test may be applied.

Clinical assessment of blemish counts (papules and pustules) change from baseline at Weeks 1, 4 and 8 will be analysed at each post-baseline visit using ANCOVA with treatment main effect, age stratum (<21, ≥21 years of age) and baseline count as covariate. Differences between least squares means for (i) test product and no treatment regimen; (ii) positive control and no treatment regimen will be presented, together with 95% confidence intervals (Table 14.2.5.1 for the ITT population and Table 14.2.5.4 for the PP population). The normality assumption for ANCOVA will be checked. If violated, non-parametric method such as Wilcoxon rank sum test may be applied. A figure will be provided for blemish profile of the ITT population (Figure 14.2.1).

The summary and analysis of lay person image assessment will be performed for polarised images and non-polarised images separately. Proportion of subjects evaluated as 'Week 8 is better' will be tabulated by treatment group and rater. Data from all 24 raters will also be pooled and a repeated measure logistic regression will be applied including effects of treatment and age stratum and exchangeable correlation structure among repeats. Odds ratio between (i) test product and no treatment regimen; (ii) positive control and no treatment regimen will be provided together with its 95%CI (Table 14.2.6.1 for polarised image, Table

14.2.7.1 for non-polarised image). This analysis will not be performed if all subjects are judged by all raters as 'Week 8 is better'.

4.5.2 Pharmacokinetic (Secondary)

Not applicable.

4.6 Analysis of Safety

4.6.1 Adverse Events and Serious Adverse Events

All adverse events (AEs) will be summarised by system organ class and preferred term.

Treatment emergent adverse events (TEAEs), defined as the AEs reported after study product application (for the untreated group, TEAE is defined as first application of the standard cleanser), will be summarized by treatment and overall including the number and percentage of subjects having AEs and total number of AEs in each SOC and preferred term (Table 14.3.1.1). TEAEs will also be tabulated by severity (Table 14.3.1.2). Treatment-related TEAEs will be summarized and presented in the same manner (Table 14.3.1.3, Table 14.3.1.4).

Deaths occurring during treatment (if any) will be listed (Listing 14.3.2.1) by treatment, including the date and study day of death, and the principal cause of death. Non-fatal serious adverse events and TEAEs causing study treatment discontinuation will be listed (Listing 14.3.2.2, 14.3.2.3).

All AEs will be listed in the Listing 16.2.7.1 for randomised subjects and Listing 16.2.7.2 for non-randomised subjects.

4.6.2 Other Safety Variables

Not applicable.

4.7 Analysis of Other Variables

Not applicable.

5 Changes to the Protocol Defined Statistical Analysis Plan

Any changes from the originally planned statistical analysis specified in the protocol are outlined in Table 1.

Table 1 Changes to Protocol Defined Analysis Plan

Protocol	Reporting & Analysis Plan	
Statistical Analysis section	**Statistical Analysis Plan**	**Rationale for Changes**
• Section 9.3.2 and Section 9.3.3	• Section 2.4.1.2 and Section 2.5	• Protocol analysis sections (9.3.2 and 9.3.3) mentions only the comparison between test product and no treatment regimen. In this SAP (Section 2.4.1.2 and Section 2.5) comparison between positive control and no treatment regimen is also included as required by client.
• Section 9.3.3	• Section 2.5	• Protocol analysis section (9.3.3) states the blemish counts will be summarized and compared between treatment groups. This has been changed in Section 2.5 of the SAP to blemish change from baseline as required by client.

Attachment 1: List of Data Displays

Study XXXX_List of Outputs.xlsx

Attachment 2: Template for Tables, Figures and Listings

This is a guideline which will give the guidance of treatment labels that will be used for the table header and in the figures, listings and in the footnotes.

The treatment labels for the column heading will be as follow:

- Test Product
- Untreated
- Positive Control

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Table 14.1.1
Subject Disposition
All Screened Subjects

All Screened Subjects (N=xxx)

	Test Product n (%)	Untreated n (%)	Positive Control n (%)	Overall n (%)
TOTAL SUBJECTS SCREENED				xxx
SUBJECTS NOT RANDOMISED				Xxx (xx.x)
DID NOT MEET STUDY CRITERIA				xxx (xx.x)
ADVERSE EVENT				Xxx (xx.x)
LOST TO FOLLOW UP				xxx (xx.x)
PROTOCOL VIOLATION				Xxx (xx.x)
WITHDRAWAL OF CONSENT				Xxx (xx.x)
OTHER				Xxx (xx.x)
SUBJECTS RANDOMISED	xxx	xxx	xxx	Xxx
COMPLETED STUDY	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
DID NOT COMPLETE STUDY	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
DID NOT MEET STUDY CRITERIA	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
ADVERSE EVENT	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
LOST TO FOLLOW-UP	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
PROTOCOL VIOLATION	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
WITHDRAWAL OF CONSENT	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
OTHER	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

	Test Product n (%)	Untreated n (%)	Positive Control n (%)	Overall n (%)
SAFETY POPULATION	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
ITT POPULATION	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
PP POPULATION	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

Programming note: For categories under 'Subjects Not Randomised' percentages will be calculated using the number of 'All Screened Subjects' as the denominator. Percentages under the 'Subjects Randomised' categories will be computed using number of subjects randomised as the denominator.

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Table 14.1.2
Incidence of Major Protocol Deviations
Randomised Population

Intent-to-Treat Population (N=xxx)

	Test Product N (%)	Untreated N (%)	Positive Control N (%)	Overall N (%)
NUMBER OF SUBJECTS WITH AT LEAST ONE MAJOR PROTOCOL VIOLATION	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
VIOLATION 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
VIOLATION 2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
VIOLATION 3	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
VIOLATION 4	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
...				

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Table 14.1.3
Analysis of Population
Randomised Population

Intent-to-Treat Population (N=xxx)

	Test Product N (%)	Untreated N (%)	Positive Control N (%)	Overall N (%)
NUMBER OF SUBJECTS EXCLUDED FROM SAFETY POPULATION	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
DEVIATION 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
DEVIATION 2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
...				
NUMBER OF SUBJECTS EXCLUDED FROM ITT POPULATION	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
DEVIATION 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
DEVIATION 2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
...				
NUMBER OF SUBJECTS WITH AT LEAST ONE DATA POINT EXCLUDED FROM PP ANALYSIS	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
NUMBER OF SUBJECTS EXCLUDED FROM PP POPULATION	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
PROTOCOL VIOLATIONS LEADING TO EXCLUSION FROM PP				
All VISITS				
DEVIATION 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
DEVIATION 2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

	Test Product N (%)	Untreated N (%)	Positive Control N (%)	Overall N (%)
...				
VISIT3 / WEEK2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
DEVIATION 3	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
DEVIATION 4	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
...				
VISIT4 / WEEK4	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
DEVIATION 5	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
DEVIATION 6	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
...				

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Table 14.1.4.1
Subject Demographics and Baseline Characteristics
Safety Population

Safety Population (N=XX)

	Test Product (N=XX)	Untreated (N=XX)	Positive Control (N=XX)	Overall (N=XX)
SEX n (%)				
MALE	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
FEMALE	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
RACE n (%)				
ASIAN	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
AFRICAN AMERICAN	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
AMERICAN INDIAN OR ALASKA NATIVE	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
WHITE	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
...(as in eCRF)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
AGE (YEARS)				
n	XX	XX	XX	XX
MEAN	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX
MEDIAN	XX.X	XX.X	XX.X	XX.X
MINIMUM	XX	XX	XX	XX

	Test Product (N=XX)	Untreated (N=XX)	Positive Control (N=XX)	Overall (N=XX)
MAXIMUM	XX	XX	XX	XX
FITZPATRICK SCALE FOR SKIN TYPE				
I	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
II	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
III	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
IV	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
V	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
VI	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
AGE STRATA (By Planned Randomisation)				
Age < 21	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Age ≥ 21	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
AGE STRATA (By Actual Age)				
Age < 21	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Age ≥ 21	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Fitzpatrick Scale I: Always burns, never tans II: Usually burns, tans minimally III: Sometimes mild burn, tans uniformly (cream white; fair with any hair or eye color) IV: Burns minimally, always tans well (moderate brown) V: very rarely burns, tans very easily (dark brown). VI Never burns, never tans (deeply pigmented dark brown to darkest brown).

Protocol 207196 Program Run Date:xxxx

Table 14.2.1
Compliance*
Intent-to-Treat Population

Intent-to-Treat Population(N=XX)

Compliance Period	Product	Test product (N=XX)		Untreated (N=XX)		Positive Control (N=XX)	
		MEAN (SD)	Median (MIN, MAX)	MEAN (SD)	Median (MIN, MAX)	MEAN (SD)	Median (MIN, MAX)
V2 to V3	Cream	x.xx(x.xxx)	x.xx(x.xx, x.xx)			x.xx(x.xxx)	x.xx(x.xx, x.xx)
	Cleanser	x.xx(x.xxx)	x.xx(x.xx, x.xx)	x.xx(x.xxx)	x.xx(x.xx, x.xx)	x.xx(x.xxx)	x.xx(x.xx, x.xx)
V3 to V4	Cream						
	Cleanser						
V4 to V5	Cream						
	Cleanser						

*Compliance = Actual Number of Uses / Expected Number of Uses

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Programming Note: For each subject, Total Expected = 2*Number of Days Between the Two Visits; Actual Uses = Expected Number – Missed Uses + Extra Uses.
For untreated group, only cleasner row to be filled.

Protocol 207196 Program Run Date:xxxx

Table 14.2.2.1
Analysis of Corneometer Change from Baseline
Intent-to-Treat Population

Intent-to-Treat Population(N=XX)

Visit	Variable	Test Product (N=XX)	Untreated (N=XX)	Positive Control (N=XX)
1 Hour Change from Baseline				
	LSmeans(SE), p-value[1]	X.xx(x.xxx), 0.xxxx	X.xx(x.xxx), 0.xxxx	X.xx (x.xxx), 0.xxxx
	Comparison[1][2]	Difference	95%CI	P-value
	Test vs Untreat	x.xx	(x.xx, x.xx)	0.xxxx
	Positive v Untreat	x.xx	(x.xx, x.xx)	0.xxxx
3 Hours Change from Baseline	(same template)			
8 Hours Change from Baseline	(Same template)			
1 Week Change from Baseline	(Same template)			
4 Week Change from Baseline	(Same template)			
8 Week Change from Baseline	(Same template)			

[1] From ANCOVA with treatment main effect, age stratum and baseline as covariate

[2] Difference is first named treatment minus second named treatment such that a negative difference favours the first named treatment

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Programming Note: If non-parametric method is used due to the failure in ANCOVA model check, the following non-parametric results should be added to the table

Comparison	P-value (Wilcoxon)
Test vs. Untreat	0.xxxx
Positive vs Untreat	0.xxxx

Protocol 207196 Program Run Date:xxxx

Table 14.2.2.2
Summary of Corneometer Change from Baseline
Intent-to-Treat Population

Intent-to-Treat Population(N=XX)

Visit	Variable	Test Product (N=XX)	Untreated (N=XX)	Positive Control (N=XX)
Baseline	n	Xx	Xx	Xx
	MEAN	x.xx	x.xx	x.xx
	SD	x.xxx	x.xxx	x.xxx
	MEDIAN	x.xx	x.xx	x.xx
	MINIMUM	X.xx	X.xx	X.xx
	MAXIMUM	X.xx	X.xx	X.xx
1 Hour				
	n	Xx	Xx	Xx
	MEAN	x.xx	x.xx	x.xx
	SD	x.xxx	x.xxx	x.xxx
	MEDIAN	x.x	x.x	x.x
	MINIMUM	X.x	X.x	X.x
	MAXIMUM	X.x	X.x	X.x
1 Hour Change from Baseline				
	n	Xx	Xx	Xx
	MEAN	x.xx	x.xx	x.xx
	SD	x.xxx	x.xxx	x.xxx

Visit		Variable	Test Product (N=XX)	Untreated (N=XX)	Positive Control (N=XX)
		MEDIAN	x.x	x.x	x.x
		MINIMUM	X.x	X.x	X.x
		MAXIMUM	X.x	X.x	X.x
3 Hours	(same template)				
3 Hours Change from Baseline	(same template)				
8 Hours	(same template)				
8 Hours Change from Baseline	(Same template)				
1 Week	(Same template)				
1 Week Change from Baseline	(Same template)				
4 Week	(Same template)				
4 Week Change from Baseline	(Same template)				
8 Week	(Same template)				
8 Week Change from Baseline	(Same template)				

Protocol 207196 Program Run Date:xxxx

Table 14.2.2.3
Summary of Corneometer Change from Baseline by Age Strata
Intent-to-Treat Population

Intent-to-Treat Population (N=XX)

Visit	Stratum	Variable	Test Product (N=XX)	Untreated (N=XX)	Positive Control (N=XX)
Baseline	Age<21	n	Xx	Xx	Xx
		MEAN	x.xx	x.xx	x.xx
		SD	x.xxx	x.xxx	x.xxx
		MEDIAN	x.xx	x.xx	x.xx
		MINIMUM	X.xx	X.xx	X.xx
		MAXIMUM	X.xx	X.xx	X.xx
	Age≥21	n	Xx	Xx	Xx
		MEAN	x.xx	x.xx	x.xx
		SD	x.xxx	x.xxx	x.xxx
		MEDIAN	x.xx	x.xx	x.xx
		MINIMUM	X.xx	X.xx	X.xx
		MAXIMUM	X.xx	X.xx	X.xx
1 Hour	Age<21	n	Xx	Xx	Xx
		MEAN	x.xx	x.xx	x.xx
		SD	x.xxx	x.xxx	x.xxx
		MEDIAN	x.xx	x.xx	x.xx
		MINIMUM	X.xx	X.xx	X.xx

Visit	Stratum	Variable	Test Product (N=XX)	Untreated (N=XX)	Positive Control (N=XX)
		MAXIMUM	X.xx	X.xx	X.xx
	Age≥21	n	Xx	Xx	Xx
		MEAN	x.xx	x.xx	x.xx
		SD	x.xxx	x.xxx	x.xxx
		MEDIAN	x.xx	x.xx	x.xx
		MINIMUM	X.xx	X.xx	X.xx
		MAXIMUM	X.xx	X.xx	X.xx
1 Hour Change from Baseline	Age<21	n	Xx	Xx	Xx
		MEAN	x.xx	x.xx	x.xx
		SD	x.xxx	x.xxx	x.xxx
		MEDIAN	x.xx	x.xx	x.xx
		MINIMUM	X.xx	X.xx	X.xx
		MAXIMUM	X.xx	X.xx	X.xx
	Age≥21	n	Xx	Xx	Xx
		MEAN	x.xx	x.xx	x.xx
		SD	x.xxx	x.xxx	x.xxx
		MEDIAN	x.xx	x.xx	x.xx
		MINIMUM	X.xx	X.xx	X.xx
		MAXIMUM	X.xx	X.xx	X.xx
3 Hour	(same template)				
3 Hours Change from	(Same template)				

Visit	Stratum	Variable	Test Product (N=XX)	Untreated (N=XX)	Positive Control (N=XX)
Baseline					
8 Hour	(same template)				
8 Hours Change from Baseline	(Same template)				
1 Week	(Same template)				
1 Week Change from Baseline	(Same template)				
4 Week	(Same template)				
4 Week Change from Baseline	(Same template)				
8 Week					
8 Week Change from Baseline	(Same template)				

Protocol 207196 Program Run Date:xxxx

Table 14.2.3.1
Analysis of Sebumeter Change from Baseline
Intent-to-Treat Population

Intent-to-Treat Population(N=XX)

Visit	Variable	Test Product (N=XX)	Untreated (N=XX)	Positive Control (N=XX)
1 Week Change from Baseline				
	LSmeans(SE), p-value	X.xx (x.xxx), 0.xxxx	X.xx (x.xxx), 0.xxxx	X.xx (x.xxx), 0.xxxx
	Comparison[1][2]	Difference	95%CI	P-value
	Test vs Untreat	x.xx	(x.xx, x.xx)	0.xxxx
	Positive vs Untreat	x.xx	(x.xx, x.xx)	0.xxxx
4 Week Change from Baseline	(same template)			
8 Week Change from Baseline	(Same template)			

[1] From ANCOVA with treatment main effect, age stratum and baseline as covariate

[2] Difference is first named treatment minus second named treatment such that a negative difference favours the first named treatment

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Table 14.2.3.2
Summary of Sebumeter Change from Baseline
Intent-to-Treat Population

Intent-to-Treat Population(N=XX)

Visit	Variable	Test Product (N=XX)	Untreated (N=XX)	Positive Control (N=XX)
Baseline	n	Xx	Xx	Xx
	MEAN	x.xx	x.xx	x.xx
	SD	x.xxx	x.xxx	x.xxx
	MEDIAN	x.xx	x.xx	x.xx
	MINIMUM	X.xx	X.xx	X.xx
	MAXIMUM	X.xx	X.xx	X.xx
1 Week	n	Xx	Xx	Xx
	MEAN	x.xx	x.xx	x.xx
	SD	x.xxx	x.xxx	x.xxx
	MEDIAN	x.xx	x.xx	x.xx
	MINIMUM	X.xx	X.xx	X.xx
	MAXIMUM	X.xx	X.xx	X.xx
1 Week Change from Baseline	n	Xx	Xx	Xx
	MEAN	x.xx	x.xx	x.xx
	SD	x.xxx	x.xxx	x.xxx
	MEDIAN	x.x	x.x	x.x

Visit		Variable	Test Product (N=XX)	Untreated (N=XX)	Positive Control (N=XX)
		MINIMUM	X.x	X.x	X.x
		MAXIMUM	X.x	X.x	X.x
4 Week	(same template)				
4 Week Change from Baseline	(Same template)				
8 Week	(Same template)				
8 Week Change from Baseline	(Same template)				

Protocol 207196 Program Run Date:xxxx

Table 14.2.3.3
Summary of Sebumeter Change from Baseline by Age Strata
Intent-to-Treat Population

Intent-to-Treat Population(N=XX)

Visit	Stratum	Variable	Test Product (N=XX)	Untreated (N=XX)	Positive Control (N=XX)
Baseline	Age<21	n	Xx	Xx	Xx
		MEAN	x.xx	x.xx	x.xx
		SD	x.xxx	x.xxx	x.xxx
		MEDIAN	x.xx	x.xx	x.xx
		MINIMUM	X.xx	X.xx	X.xx
		MAXIMUM	X.xx	X.xx	X.xx
	Age≥21	n	Xx	Xx	Xx
		MEAN	x.xx	x.xx	x.xx
		SD	x.xxx	x.xxx	x.xxx
		MEDIAN	x.xx	x.xx	x.xx
		MINIMUM	X.xx	X.xx	X.xx
		MAXIMUM	X.xx	X.xx	X.xx
1 Week	Age<21	n	Xx	Xx	Xx
		MEAN	x.xx	x.xx	x.xx
		SD	x.xxx	x.xxx	x.xxx
		MEDIAN	x.xx	x.xx	x.xx
		MINIMUM	X.xx	X.xx	X.xx

Visit	Stratum	Variable	Test Product (N=XX)	Untreated (N=XX)	Positive Control (N=XX)
		MAXIMUM	X.xx	X.xx	X.xx
	Age≥21	n	Xx	Xx	Xx
		MEAN	x.xx	x.xx	x.xx
		SD	x.xxx	x.xxx	x.xxx
		MEDIAN	x.xx	x.xx	x.xx
		MINIMUM	X.xx	X.xx	X.xx
		MAXIMUM	X.xx	X.xx	X.xx
1 Week Change from Baseline					
	Age<21	n	Xx	Xx	Xx
		MEAN	x.xx	x.xx	x.xx
		SD	x.xxx	x.xxx	x.xxx
		MEDIAN	x.xx	x.xx	x.xx
		MINIMUM	X.xx	X.xx	X.xx
		MAXIMUM	X.xx	X.xx	X.xx
	Age≥21	n	Xx	Xx	Xx
		MEAN	x.xx	x.xx	x.xx
		SD	x.xxx	x.xxx	x.xxx
		MEDIAN	x.xx	x.xx	x.xx
		MINIMUM	X.xx	X.xx	X.xx
		MAXIMUM	X.xx	X.xx	X.xx
4 Week	(Same template)				

Visit	Stratum	Variable	Test Product (N=XX)	Untreated (N=XX)	Positive Control (N=XX)
4 Week Change from Baseline	(Same template)				
8 Week	(Same template)				
8 Week Change from Baseline	(Same template)				

Protocol 207196 Program Run Date:xxxx

Table 14.2.6.1
Analysis of Lay Person Assessment Polarised Image
Intent-to-Treat Population

Intent-to-Treat Population(N=XX)

Variable	Test Product (N=XX)	Untreated (N=XX)	Positive Control (N=XX)
ODDS[1]	xx.xx	Xx.xx	Xx.xx

Comparison[1][2]	ODDS RATIO	95%CI	p-value
Test vs. Control	xx.xx	(xx.xx, xx.xx)	0.xxxx

ODDS=p/(1-p) where p is the probability of event that week 8 is better than baseline.
[1] From logistic regression including treatment and age stratum effects and exchangeable correlation structure among repeats

[2] Odds ratio is the first named treatment over the second named treatment such that ratio > 1 favours the first named treatment

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Protocol 207196 Program Run Date:xxxx

Table 14.2.6.2
Summary of Lay Person Assessment Polarised Image by Rater
Intent-to-Treat Population

Intent-to-Treat Population(N=XX)

Rater	Number of Subjects Assessed	Variable	Test Product (N=XX)	Untreated (N=XX)	Positive Control (N=XX)
01	xx	Proportion (Week 8 is better)	Xx.x%	Xx.x%	Xx.x%
02	xx	Proportion (Week 8 is better)	Xx.x%	Xx.x%	Xx.x%
...					
24	xx	Proportion (Week 8 is better)	Xx.x%	Xx.x%	Xx.x%

Protocol 207196 Program Run Date:xxxx

Table 14.3.1.1
Treatment Emergent Adverse Event by System Organ Class and Preferred Term
Safety Population

Safety Population (N=xx)

System Organ Class Preferred Term	Test Product (N=XX)		Untreated (N=XX)	Positive Control (N=xx)	Overall (N=XX)	
	n (%)	nAE			n (%)	nAE
NUMBER OF SUBJECTS WITH AT LEAST ONE TEAE	xx (xx.x)	xx	... ...	... ...	xx (xx.x)	xx
NUMBER OF SUBJECTS WITH NO TEAE	xx (xx.x)	xx	... ...	... ...	xx (xx.x)	xx
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	xx (xx.x)	xx	... ...	... ...	xx (xx.x)	xx
ERYTHEMA	xx (xx.x)	xx	... ...	... ...	xx (xx.x)	xx
DERMATITIS	xx (xx.x)	xx	... ...	... ...	xx (xx.x)	xx
GASTROINTESTINAL SYSTEM	xx (xx.x)	xx	... ...	... ...	xx (xx.x)	xx
ABDOMINAL PAIN	xx (xx.x)	xx	... ...	... ...	xx (xx.x)	xx
DRY MOUTH	xx (xx.x)	xx	... ...	... ...	xx (xx.x)	xx
VOMITTING	xx (xx.x)	xx			xx (xx.x)	xx

n (%) = Number (percent) of subjects nAE = Number of adverse events.

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Protocol 207196 Program Run Date:xxxx

Table 14.3.1.2
Treatment Emergent Adverse Event by System Organ Class, Preferred Term and Severity
Safety Population

Safety Population (N=xx)

System Organ Class Preferred Term	Test Product (N=XX)						...	Overall (N=XX)					
	Mild		Moderate		Severe			Mild		Moderate		Severe	
	n (%)	nAE	n (%)	nAE	n (%)	nAE		n (%)	nAE	n (%)	nAE	n (%)	nAE
NUMBER OF SUBJECTS WITH AT LEAST ONE TEAE	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	...	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
		xx		xx		xx	...		xx		xx		xx
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx		xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
ERYTHEMA	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	...	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
DERMATITIS	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	...	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
GASTROINTESTINAL SYSTEM	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	...	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
ABDOMINAL PAIN	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	...	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
DRY MOUTH	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	...	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
VOMITTING	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	...	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx

n (%) = Number (percent) of subjects nAE = Number of adverse events.

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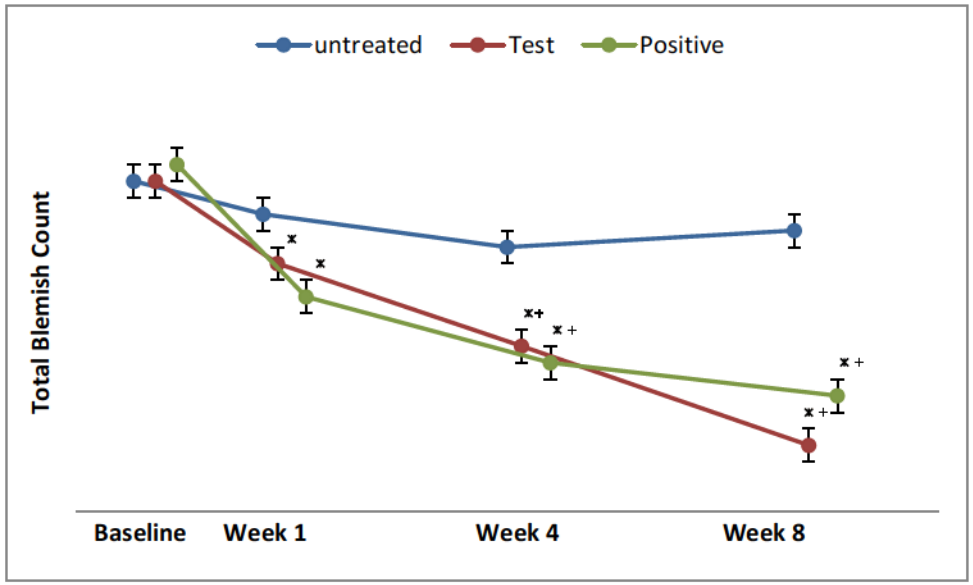
Figure 14.2.1
Total Blemish Count Mean (±SE) Plot Over Time by Treatment
Intent-to-Treat Population

Intent-to-Treat Population (N=XX)



* Significant change from baseline within group (p<0.05)
+ Significant treatment difference on change from baseline as compared to untreated (p<0.05)

Protocol 207196 Program Run Date:xxxx

Listing 16.1.7
Randomisation Information
Randomised Population

Stratum 1: Age<21 Seed: xxxxxx Block Size: x

Subject Number	Age/Sex/Race[1]	Randomisation Number	Treatment Randomised	Date of Randomisation
PPD	32/F/W	PPD		20-Mar-2017

[1] Age in years; Sex: F = Female, M = Male ; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, O = Multiple.

Protocol 207196 Program Run Date:xxxx

Listing 16.2.1.1
Subject Disposition
Randomised Population

Treatment Group: Test Product

Subject	Age/Sex/ Race [1]	Screening date	Treatment Start Date and Time	Date of Completion or withdrawal	Duration of Treatment (Days)	Completed (Yes/No)	Primary Reason for Withdrawal
PPD							
….							

[1] Age in years; Sex: F = Female, M = Male; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, M = Multiple.

Protocol 207196 Program Run Date:xxxx

Listing 16.2.1.2
Subject Disposition
Non-Randomised Subjects

Subject Number	Age/Sex/ Race [1]	Screening date	Reason of Screen failure
PPD			

[1] Age in years; Sex: F = Female, M = Male; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, M = Multiple.

Protocol 207196 Program Run Date:xxxx

Listing 16.2.2.1
Major Protocol Deviations
All Randomized Subjects

Treatment Group: XXXXXX

Subject	Sex/Age/ Race [1]	Week(s)/Time(s) Excluded from PP Population	Deviation Reason
PPD			

[1] Age in years; Sex: F = Female, M = Male; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, M = Multiple.

Protocol 207196 Program Run Date:xxxx

Listing 16.2.2.2
Minor Protocol Deviation
Randomised Population

Treatment Group: Test Product

Subject Number	Age/Sex/Race[1]	Visit	Deviation Sequence	Protocol Deviation
PPD				xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

[1] Age in years; Sex: F = Female, M = Male ; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, O = Multiple.

Protocol 207196 Program Run Date:xxxx

Listing 16.2.3.1
Exclusions from Analysis Populations
Randomised Population

Treatment Group: Test Product

Subject Number	Age/Sex/Race[1]	Treatment Start Date and Time	Safety Population (Yes/No)	ITT Population (Yes/No)	PP population (Yes/No)
PPD					

[1] Age in years; Sex: F = Female, M = Male ; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, O = Multiple.

Protocol 207196 Program Run Date:xxxx

Listing 16.2.4.1
Demographic Characteristics
Randomised Population

Treatment Group: Test Product

Subject Number	Age (years)	Sex	Race	Fitzpatrick Skin Type	Stratum (Planned)	Stratum (Actual)
PPD						

Protocol 207196 Program Run Date:xxxx

Listing 16.2.4.2
Medical History and Current Medical Conditions
Randomised Population

Treatment Group: Test Product

Subject	Age/Sex/Race [1]	Any Medical History? (Yes/No)	Medical Condition	Start Date	Ongoing? (Yes/No)	End Date
PPD						

[1] Age in years; Sex: F = Female, M = Male; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, M = Multiple.

Protocol 207196 Program Run Date:xxxx

Listing 16.2.5.1
Study Product Administration and Compliance
Randomised Population

Treatment Group: Test Product

Subject Number	Age/Sex/Race[1]	Administration (Yes/No)	Compliance period	Days in Period	Product	Number Missed	Number Extra
PPD							

[1] Age in years; Sex: F = Female, M = Male; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, M = Multiple.

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Listing 16.2.5.2
Concomitant medications and significant non-drug therapies taken during treatment
Randomised Population

Treatment Group: Test Product

Subject Number	Age/Sex/Race[1]	Sequence Number	Treatment	Reason of Treatment	Frequence	Start Date	Ongoing? (Yes/No)	End Date (Ongoing)
PPD								

[1] Age in years; Sex: F = Female, M = Male; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, M = Multiple.

Protocol 207196 Program Run Date:xxxx

Listing 16.2.6.1
Corneometer Measurement
Randomised Population

Treatment Group: Test Product

Subject Number	Age/Sex/Race[1]	Visit	Time	Measurement 1	Measurement 2	Measurement 3	Mean	Mean Change from Baseline
PPD								

[1] Age in years; Sex: F = Female, M = Male; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, M = Multiple.

Protocol 207196 Program Run Date:xxxx

Listing 16.2.6.2
Sebumeter and Sebumeter Kinetic Measurements
Randomised Population

Treatment Group: Test Product

Subject Number	Age/Sex/Race[1]	Visit	Time	Measurement 1	Measurement 2	Measurement 3	Mean	Mean Change from baseline
PPD								

[1] Age in years; Sex: F = Female, M = Male; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, M = Multiple.

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PPD

Protocol 207196 Program Run Date:xxxx

Listing 16.2.6.3
Blemish Count
Randomised Population

Treatment Group: Test Product

Subject Number	Age/Sex/Race[1]	Visit	Papules (Forehead, Cheeks, Chin)	Pustules (Forehead, Cheeks, Chin)	Total	Total Change from Baseline
PPD						

[1] Age in years; Sex: F = Female, M = Male; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, M = Multiple.

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PPD

Protocol 207196 Program Run Date:xxxx

Listing 16.2.6.4
Image assessment
Randomised Population

Treatment Group: Test Product

Subject Number	Age/Sex/Race[1]	Compare	Rater	Image	Score[2]
PPD					

[1] Age in years; Sex: F = Female, M = Male; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, M = Multiple.
[2] Score: 0= Day1 image is better, 1= Day57 image is better.

Protocol 207196 Program Run Date:xxxx

Listing 16.2.7.1
All Adverse Events
Randomised Population

Treatment Group: Test Product

Subject Number	Age/Sex/ Race[1]	Adverse Event (Preferred Term) (System Organ Class)	Start Date /Study Day[2]	Start Time	End Date	End Time	Frequency /Intensity [3]	Related to Study Product?	Action Taken re Study Product	Outcome	Serious?	Withdrew? [4]
PPD												

[1] Age in years; Sex: F = Female, M = Male ; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, O = Multiple.
[2] Study day is the day relative to start of treatment, day 1 being the day of first treatment.
[3] INT = Intermittent and SGLE = Single.

[4] Did subject withdraw from study as a result of this adverse event?

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PPD

Programming Note for Listing 16.2.7.2:

Repeat the same layout for listing 16.2.7.2

Population should be used 'Non randomised Subjects'

The fourth column should be only 'Start Date'

Delete the footnote related to study day and adjust the numbers accordingly.

GlaxoSmithKline
Consumer Healthcare

STATISTICAL REPORTING AND ANALYSIS PLAN ADDENDUM 1

A randomised, parallel-group, evaluator-blind, no-treatment and positive controlled, single-site, proof of concept clinical study to evaluate the cosmetic benefit provided by 8 weeks of twice-daily topical application of a developmental moisturising cream with niacinamide in healthy subjects with sensitive, oily, blemish-prone skin

Protocol Number: 207196

Phase: NA

Document History

Document	Version Date	Summary of Changes (New analysis or Change in planned analysis)
Addendum 1	20-Dec-2017	In addition to the planned analysis on lay rater image data as in RAP Section 4.5.1, an ANOVA on combined rate (over 24 raters) will be performed as requested by client. Table shell T 14.2.6.3 and T 14.2.7.3 are created for the ANOVA analysis of polarised image and non-polarised image respectively.
Original Analysis Plan	19-Sept-2017	Not applicable (N/A)

Table of contents

1 Introduction

This RAP addendum describes an analysis and its outputs in addition to those planned in the Statistical Reporting and Analysis Plan (V1.0, 19-Sept-2017) and Study protocol (V4.0, 23-May-2017). This analysis was requested by client after study unblinding but prior to final CSR. This additional analysis will be reported in the final CSR.

The sections below provide the updated text to that of the RAP Section 4.5 for the analyses of the secondary objectives, with Section 5.0 providing further details on what was planned, the additional and the reason for the additional. A summary of the additional analysis is as the following.

Lay person assessment of the appearance of blemishes was one of the secondary endpoints of the study. There were 24 raters and each gave a score 1 or 0 to each subject (indicating if Week 8 image was better than baseline image or not). An additional analysis on this endpoint was requested by client to average the 24 rating scores within a subject and then apply an ANOVA analysis to the average rates of all subjects including effects of treatment and age stratum.

4.5 Analysis of Secondary Objectives

4.5.1 Efficacy

The summary and analysis of lay person image assessment will be performed for polarised images and non-polarised images separately. Proportion of subjects evaluated as 'Week 8 is better' will be tabulated by treatment group and rater. Data from all 24 raters will also be pooled and a repeated measure logistic regression will be applied including effects of treatment and age stratum and exchangeable correlation structure among repeats. Odds ratio between (i) test product and no treatment regimen; (ii) positive control and no treatment regimen will be provided together with its 95%CI (Table 14.2.6.1 for polarised image, Table 14.2.7.1 for non-polarised image). This analysis will not be performed if all subjects are judged by all raters as 'Week 8 is better'.

Here 'Week 8 is better' implies Week 8 shows less blemishes than baseline.

Data from all 24 raters for each subject will be combined into average rate - the mean of missing scores from 24 raters. An ANOVA analysis will then be applied with factors for treatment and age stratum. Mean treatment responses and differences between (i) test product and no treatment regimen; (ii) positive control and no treatment regimen will be provided together with 95%CIs (Table 14.2.6.3 for polarised image, Table 14.2.7.3 for non-polarised image, ITT population).

5 Changes to Statistical Analysis Plan

There is no change to the planned analysis in RAP (dated 19 Sept 2017). An additional analysis is added as outlined in Table 1.

Table 1 Additional to RAP Defined Analysis Plan

Analysis in RAP	Additional in RAP addendum	Rationale for the additional
• Last Paragraph of Section 4.5.1 The summary and analysis of lay person image assessment will be performed for polarised images and non-polarised images separately. Proportion of subjects evaluated as 'Week 8 is better' will be tabulated by treatment group and rater. Data from all 24 raters will also be pooled and a repeated measure logistic regression will be applied including effects of treatment and age stratum and exchangeable correlation structure among repeats. Odds ratio between (i) test product and no treatment regimen; (ii) positive control and no treatment regimen will be provided together with its 95%CI (Table 14.2.6.1 for polarised image, Table 14.2.7.1 for non-polarised image). This analysis will not be performed if all subjects are judged by all raters as 'Week 8 is better'	• Last two Paragraphs of Section 4.5.1 The summary and analysis of lay person image assessment will be performed for polarised images and non-polarised images separately. Proportion of subjects evaluated as 'Week 8 is better' will be tabulated by treatment group and rater. Data from all 24 raters will also be pooled and a repeated measure logistic regression will be applied including effects of treatment and age stratum and exchangeable correlation structure among repeats. Odds ratio between (i) test product and no treatment regimen; (ii) positive control and no treatment regimen will be provided together with its 95%CI (Table 14.2.6.1 for polarised image, Table 14.2.7.1 for non-polarised image). This analysis will not be performed if all subjects are judged by all raters as 'Week 8 is better'. Here 'Week 8 is better' implies Week 8 shows less blemishes than baseline. Data from all 24 raters for each subject will be combined into average rate, An ANOVA analysis will then be applied including effects of treatment	GSKCH requested an additional analysis due to the following observations. (i) In the planned repeated measurement logistic analysis, correlation structure among repeated assessments could have different choices and the robustness of the results with respect to different choices of correlation was unsure. (ii) Treatment evaluation and treatment comparison in terms of odds and oddsratio in the planned analysis were not as intuitive as rate and rate difference. An alternative would be to remove the correlation by combining the 24 rating scores within a subject to get an average rating for the subject (equivalent to proportion of raters who rate W8 image of the subject better than the baseline image).

Analysis in RAP	Additional in RAP addendum	Rationale for the additional
	and age stratum. Treatment differences on average rate between (i) test product and no treatment regimen; (ii) positive control and no treatment regimen will be provided together with its 95%CI (Table 14.2.6.3 for polarised image, Table 14.2.7.3 for non-polarised image, ITT population).	

Attachment Template for Table

Protocol 207196 Program Run Date:xxxx

Table 14.2.6.3
Analysis of Lay Person Assessment Combined Rating for Polarised Image
Intent-to-Treat Population

Intent-to-Treat Population(N=XX)

Visit	Variable	Test Product (N=XX)	Untreated (N=XX)	Positive Control (N=XX)
Week 8	LSmeans(SE)[1]	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)

Comparison[1][2]	Difference	95%CI	p-value
Test vs. Untreated	x.xx	(x.xx, x.xx)	0.xxxx
Positive vs. Untreated	x.xx	(x.xx, x.xx)	0.xxxx

[1] From ANOVA on average rate over all raters including effects of treatment and age stratum.

[2] Difference is the first named treatment minus the second named treatment such that a positive difference favours the first named treatment

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Protocol 207196 **Program Run Date:xxxx**

Table 14.2.7.3
Analysis of Lay Person Assessment Combined Rating for Non-Polarised Image
Intent-to-Treat Population

Intent-to-Treat Population(N=XX)

Visit	Variable	Test Product (N=XX)	Untreated (N=XX)	Positive Control (N=XX)
Week 8	LSmeans(SE)[1]	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)

Comparison[1][2]	Difference	95%CI	p-value
Test vs. Untreated	x.xx	(x.xx, x.xx)	0.xxxx
Positive vs. Untreated	x.xx	(x.xx, x.xx)	0.xxxx

[1] From ANOVA on average rate over all raters including effects of treatment and age stratum.

[2] Difference is the first named treatment minus the second named treatment such that a positive difference favours the first named treatment

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CCI CCI