STATISTICAL REPORTING AND ANALYSIS PLAN

A Clinical Study to Assess the Cutaneous and Ocular Local Tolerance of Two Cosmetic Facial Cleansers in Healthy Females with Sensitive Skin Under Normal Conditions of Use

Protocol Number: 207782

Phase: N/A

Document History

Document	Version Date	Summary of Changes (New analysis or Change in planned analysis)
Amendment 1	14-Aug-2017	Added new mandatory listings and incorporated in new template.
Original Analysis Plan	30-Jun-2017	Not applicable (N/A)

Amendments incorporate all revisions to date.

Table of contents

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 207782.

1 Summary of Key Protocol Information

The objective of this clinical study is to assess the cutaneous and ocular local tolerance of two cosmetic facial cleansers in healthy females with sensitive skin under normal conditions of use.

1.1 Study Design

Overall Design
This is an assessor blind (dermatologist and ophthalmologist) clinical in use study to determine the local cutaneous and ocular tolerance of two cosmetic facial cleanser products when used as per the intended instructions for use in a population of healthy female subjects with clinically assessed sensitive skin. Subjects who have sensitive skin as classified by a positive reaction to a lactic acid Stinging Test will be asked to use one of two cleansing products as part of their normal skin care routine for 3 weeks. Both test products are the same formulation but are differentiated by the dispensing pack; to either a micellar cleanser or a foaming cleanser. Subjects will be instructed to cleanse their face with one of the two test products at home twice-daily, for 21 (+ 2) days, including a supervised first application at the study site (Visit 2) and a final application at home on the morning of the final visit (Visit 3), as per the intended instructions for use. A qualified dermatologist and a qualified ophthalmologist will assess the baseline cutaneous and ocular irritation of prospective subjects at Visit 2. For a subject to be considered eligible to participate in the study, all dermatologist and ophthalmologist assessment scores must be zero. Further dermatologist and ophthalmologist assessments will be completed 1-hour (± 20 minutes) post supervised first product use and at the final visit (Visit 3) at the end of the 21 (+2) day product use period. The intensity of any visual signs of cutaneous and ocular irritation will be recorded by the dermatologist and ophthalmologist, according to the assessment scales detailed in section 2.4.1. The dermatologist will also determine each subject's facial skin type as dry, oily or normal/combination skin. Any subject classified as having oily skin will not be considered eligible for participation in the study as they do not represent the target population for the product. Subjects will be asked to complete self-assessment questions at Visit 2 prior to any study product use (section 2.4.2). In addition, randomized subjects will be asked to complete the self- assessment questions 1 hour (± 20 minutes) post supervised first product use and at the end of the 21 (+2) day product use period.

The objective of this clinical study is to assess the cutaneous and ocular local tolerance of two cosmetic facial cleansers in healthy females with sensitive skin under normal conditions of use.

Visit 1 – Screening Visit

The following assessments will be conducted:

1. Subject Informed Consent taken
2. Subject demographics collected
3. Medical history details collected
4. Details of current and concomitant medication collected
5. Inclusion/Exclusion criteria
6. Contact lens wearer status assessment (Yes or No)
7. Clinical diagnosis of sensitive skin confirmed by Lactic Acid sting test
8. Determination of subject eligibility to participate in the study
9. Adverse events will be reported following the Lactic Acid stinging test procedure

Visit 2 – Baseline Visit

Within 7 days of the Screening Visit

The following assessments will be conducted:

1. Current/Concomitant medications review
2. **INCLUSION/EXCLUSION CRITERIA**
3. Fitzpatrick skin type assessment
4. Dermatologist assessment of skin type status (dry, oily or normal/combination) Inclusion criteria 5e and Exclusion criteria 7f
5. Clinical dermatologist assessment for eligibility to participate in the study (including visual examinations). Inclusion criteria 5c
   Note: subject must have a total score of zero for inclusion into the study
6. Clinical ophthalmologist assessment for eligibility to participate in the study (including visual examinations). Inclusion criteria 5d
   Note: subject must have a total score of zero for inclusion into the study.
7. Subject self-assessment questions. Prior to product use.
8. Continued eligibility check
9. Randomization and stratification
10. Dispense assigned study product and diary card/instructions for use
11. Supervised first use of assigned product
12. Dermatologist (Appendix 3) and ophthalmologist assessments 1 hour (± 20 minutes) post supervised first product application
13. Subject self-assessment questions 1 hour (± 20 minutes) post first supervised

use 14. Adverse events assessment
Visit 3 - Week 3 / Exit from Study (21 (+ 2) Days)
The following assessments will be conducted: 1. Current/Concomitant medications review 2. Continued eligibility check 3. Return study product and diary card/instructions for use 4. Diary card check to confirm compliant product use 5. Dermatologist final assessment of tolerance (Appendix 3) 6. Ophthalmologist final assessment of tolerance (Appendix 4) 7. Subject final self-assessment questions (Appendix 5) 8. Adverse event assessment 9. Subject discharge from the study site following completion of all study procedures

1.2 Study Objectives

Objectives	Endpoints
Primary Objective	**Primary Endpoint**
• Assessment of the cutaneous and ocular tolerance of two cosmetic facial cleansers after 21 (+ 2) days of product use per the intended instructions in healthy female subjects with clinically assessed sensitive skin.	• Dermatologist and ophthalmologist visual assessment of cutaneous and ocular irritation after 21 (+ 2) days of test product use.
Secondary Objectives	**Secondary Endpoints**
Assessment of the cutaneous and ocular tolerance of two cosmetic facial cleansers on Day 1 of product use per the intended instructions in healthy female subjects with clinically assessed sensitive skin.	Dermatologist and ophthalmologist visual assessment of cutaneous and ocular irritation on Day 1 of test product use.
• Assessment of the cutaneous and ocular tolerance of two cosmetic facial cleansers after 21 (+ 2) days of product use per the intended instructions in healthy female subjects with clinically assessed sensitive skin.	• Subject self-assessment question responses (redness, dryness, burning, itching and stinging) with regards to product use experience on the face and around the eyes after 21 (+ 2) days of test product use.
• To evaluate the general safety of two cosmetic facial cleansers.	• Frequency and severity of Adverse Events

1.3 Treatments

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

	Test Product 1	Test Product 2
Product Name	Micellar Cleanser	Micellar Foaming Cleanser
Product Formulation Code (MFC)	CCI [redacted]	
Product Format	200ml Clear plastic bottle	150ml Plastic pump pack
Application Quantity	To be used as per normal home use application	
Route of Administration	Topical dermal application	
Application Instructions	Use morning and evening. Apply to a cotton pad and wipe over the entire face and closed eyes to gently cleanse. No need to rub or rinse. Cotton pads will be supplied.	Use morning and evening. Massage gently onto wet skin on the face using fingertips, rinse thoroughly and pat skin dry.

1.4 Sample Size Calculation

A sufficient number of subjects will be screened (up to 170) to randomize approximately 92 subjects (46 per treatment group) to ensure that at least 40 subjects in each treatment group complete the study (80 subjects in total).

Randomization will be stratified by both contact lens wearer status (yes or no) and skin type (dry or normal/combination). The aim is to ensure balance of strata effects between treatment groups.

The sample size is based on clinical considerations to provide descriptive information on the tolerability and safety of the products, and is consistent with ANVISA guidelines (ANVISA, 2012).

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 pre-treatment assessment with a non-missing value.

Unless otherwise stated, if baseline data is missing no derivation will be performed and will be set to missing.

3.2 Subgroups/Stratifications

Subjects are randomised by two strata, contact lens wearer (Yes or No) and cosmetic skin type (dry or normal/combination). Efficacy variables will be analysed accounting for strata.

4 Data Analysis

Data analysis will be performed by inVentiv Health Clinical. The statistical analysis software used will be SAS version 9.4 (Studio).

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.

Except as described below, all listings will be produced for all randomized subjects.

4.1 Populations for Analysis

Tables described in this section other than disposition will be produced for all randomized subjects.

4.1.1 Subject Disposition

Screen failures will be defined as subjects who do not satisfy all the inclusion/exclusion criteria. A summary will be provided of the number of subjects screened and the number of screen failures with reasons why subjects were not randomized.

Subject disposition will be summarized 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 summarize the number and percent of subjects assigned to each analysis population (refer to section 4.1.3).

Subject disposition including the subject status (completer, Yes/No), critical demographic data (age, sex, race), the duration of treatment before discontinuation and the specific reason for discontinuation, will be listed in Listing 16.2.1.1. by treatment group.

4.1.2 Protocol Deviations

Protocol violations will be tracked by the study team throughout the conduct of the study. A per protocol analysis is not planned for this study, but data will be reviewed prior to unblinding and closure of the database.

All-important violations will be defined in the "Review Listing Requirement (RLR)" document.

A list of protocol deviations will be provided in Listing 16.2.2.

4.1.3 Analysis Populations

Two analysis populations are defined.

Population	Definition / Criteria	Analyses Evaluated
Safety	• Comprises of all subjects for whom the lactic acid stinging test was performed. • This population will be based on the treatment the subject actually received.	• Safety
Intent-To-Treat	• Comprises of all randomized subjects who have at least one cutaneous or ocular assessment following study product application. • This population will be based on the treatment the subject is randomised to.	• Efficacy

NOTES :

- Please refer to Attachment 1: List of Data Displays which details the population to be used for each displays being generated.

4.2 Subject Demographics and Other Baseline Characteristics

Demographic and baseline characteristics summaries will be produced for the ITT and Safety populations by treatment group.

4.2.1 Demographic Characteristics

These summaries will include age, gender, race and strata. It will also include Fitzpatrick skin type. Categorical measures (gender, race, contact lens wearer status, Fitzpatrick skin type and

cosmetic skin type) will be summarised by the number and percentage of subjects in each category. Descriptive statistics for age will include the mean, median, standard deviation and minimum/maximum.

4.2.2 General Medical History

Medical history data will not be presented in the study report. A data listing will be produced only at the blinded data review stage.

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

4.3.1 Study Product/Drug Compliance and Exposure

Treatment compliance (number of missed uses and number of additional uses) will be listed for the blinded data review.

4.3.2 Prior and Concomitant Medication

Prior and concomitant medications and concomitant non-drug treatment will be listed for the blinded data review.

4.4 Analysis of Efficacy

4.4.1 Primary Efficacy Endpoint

4.4.1.1 Primary Efficacy Endpoint Definition

The primary endpoints are the dermatologist and ophthalmologist assessments of local tolerance through visual assessment of cutaneous (dermal response and superficial irritation) and ocular (conjunctiva involvement and lacrimal intensity) irritation scores/grades at Day 21.

This study will be considered a success if the majority (i.e. >50%) of subjects per treatment arm with combined dermatologist and ophthalmologist scores of zero at day 21 (+ 2).

Calculation of combined dermatologist score (dermal response and superficial irritation):

The combined dermatologist score will be calculated in the following way:

Combined score = dermal response score + numerical equivalent of the superficial irritation score

Where, the dermal response scale is described in the Table 1 below, and the superficial irritation scores in Table 2 below.

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[redacted]

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[redacted]

4.4.1.2 Statistical Hypothesis, Model, and Method of Analysis

No formal statistical inference will be performed.

The combined dermatologist and ophthalmologist score will be summarized using frequencies and percentages by treatment group and time point, with Day 21 results of primary interest. The sum across post-baseline observations for the combined dermatologist and

ophthalmologist score will also be summarized using frequencies and percentages by treatment group.

Similar summaries will also be provided for the following variables:

- Combined dermatologist and ophthalmologist score (modified) = dermal response score + conjunctiva involvement score + lacrimal intensity score
- Combined dermatologist score
- Combined ophthalmological score
- Dermal response score
- Conjunctiva involvement score
- Lacrimal intensity score

Data will also be presented by sub-groups (strata), contact lens wearer status (not contact lens wearer, contact lens wearer) and skin type (dry, normal/combination) by the following categories:

- Not contact lens wearer with dry skin
- Contact lens wearer with dry skin
- Not contact lens wearer with normal/combination skin
- Contact lens wearer with normal/combination skin.

4.4.2 Secondary Efficacy Variables

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[redacted]

4.5 Analysis of Secondary Objectives

4.5.1 Efficacy (Secondary)

The secondary endpoints will be summarized in the same way as the primary endpoints. Each subject assessment (redness, dryness, burning, itching and stinging) and combined score (summed across these 5 assessments) will be presented at each time point separately for eyes and face. The sum across post-baseline observations will also be summarized in the same way.

4.6 Analysis of Safety

4.6.1 Adverse Events and Serious Adverse Events

All adverse events (AEs) will be summarised by primary system organ class and preferred term according to the current version of the MedDRA.

Treatment emergent adverse events (TEAEs) will be summarized by the number and percentage of subjects having any adverse event, an adverse event in each System Organ Class, and each individual adverse event (Table 14.3.1.1). All TEAEs will also be tabulated by severity (Table 14.3.1.2). Treatment-emergent AEs suspected of a relationship to study product will be presented in a similar manner (Table 14.3.1.3). For treatment-related AEs, these will also be presented by severity (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. Serious adverse events leading to discontinuation will be listed (Listing 14.3.2.2).

All AEs will be listed in the Listing 16.2.7.1 and Listing 16.2.7.2.

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 (dated 26-May-2017) are outlined in Table 1.

Table 1 Changes to Protocol Defined Analysis Plan

Protocol	Statistical Analysis Plan	Rationale for Changes
• Section 2 – Objectives and Endpoints	• Section 1.2 Study Objectives. The dermatologist and ophthalmologist visual assessment of cutaneous and ocular irritation objective/endpoint at Day 1 has been added as a secondary objective.	• For clarification that the Day 21 is the primary endpoint of interest, whereas the Day 1 results are of secondary importance.
• Section 9.2.3 - Criteria for Evaluation of Local Tolerance. "This study will be considered a success if the majority (i.e. >50%) of subjects per treatment arm complete the study with combined dermatologist and ophthalmologist scores of zero at day 21 (+ 2)."	• Section 4.4.1.1 - Primary efficacy endpoint definition. Reference to subjects completing the study has been removed.	• Requirement for subjects to complete the study is not applicable when assessing the success of the study. This was specified in error in the protocol. The analysis population definition has no requirement for subjects to complete the study for evaluability.

6 Top-line Summary

The following outputs will be produced for the top-line report.

Table/Listing/Figure No.	Title
Table 14.1.1	Subject Disposition
Table 14.2.1.1	Frequency of Combined Dermatologist and Ophthalmologist Score – Intent To Treat Population
Table 14.3.1.1	Treatment Emergent Adverse Events by System Organ Class and Preferred Term – Safety Population
Table 14.2.3.1	Frequency of Combined Dermatologist Score – Intent To Treat Population
Table 14.2.4.1	Frequency of Combined Ophthalmological Score – Intent To Treat Population

Attachment 1: List of Data Displays

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7 List of Tables, Figures and Listings

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

1) Micellar Cleanser

2) Micellar Foaming Cleanser

Table No.	Table Title (including population)	Template
14.1.1	Subject Disposition	Section 6
14.1.2.1	Demographic Characteristics – Safety Population	Section 6
14.1.2.2	Demographic Characteristics – Intent To Treat Population	Table 14.1.2.1
14.2.1.1	Frequency of Combined Dermatologist and Ophthalmologist Score– Intent To Treat Population	Section 6
14.2.1.2	Frequency of Combined Dermatologist and Ophthalmologist Score by Strata – Intent To Treat Population	Table 14.2.1.1
14.2.2.1	Frequency of Combined Dermatologist and Ophthalmologist Score (Modified) – Intent To Treat Population	Table 14.2.1.1
14.2.2.2	Frequency of Combined Dermatologist and Ophthalmologist Score (Modified) by Strata – Intent To Treat Population	Table 14.2.1.1
14.2.3.1	Frequency of Combined Dermatologist Score – Intent To Treat Population	Table 14.2.1.1

14.2.3.2	Frequency of Combined Dermatologist Score by Strata – Intent To Treat Population	Table 14.2.1.1
14.2.4.1	Frequency of Combined Ophthalmological Score – Intent To Treat Population	Table 14.2.1.1
14.2.4.2	Frequency of Combined Ophthalmological Score by Strata – Intent To Treat Population	Table 14.2.1.1
14.2.5.1	Frequency of Dermal Response Score – Intent To Treat Population	Section 6
14.2.5.2	Frequency of Dermal Response Score by Strata – Intent To Treat Population	Table 14.2.5.1
14.2.6.1	Frequency of Conjunctiva Involvement Score – Intent To Treat Population	Section 6
14.2.6.2	Frequency of Conjunctiva Involvement Score by Strata – Intent To Treat Population	Table 14.2.6.1
14.2.7.1	Frequency of Lacrimal Intensity Score – Intent To Treat Population	Table 14.2.5.1
14.2.7.2	Frequency of Lacrimal Intensity Score by Strata – Intent To Treat Population	Table 14.2.5.1
14.2.8.1	Frequency of Subject Assessment Scores for Eyes - Intent to Treat Population	Section 6
14.2.8.2	Frequency of Subject Assessment Combined Score for Eyes - Intent to Treat Population	Section 6
14.2.9.1	Frequency of Subject Assessment Scores for Face - Intent to Treat Population	Table 14.2.8.1
14.2.9.2	Frequency of Subject Assessment Combined Score for Face - Intent to Treat Population	Table 14.2.8.2
14.3.1.1	Treatment Emergent Adverse Events by System Organ Class and Preferred Term – Safety Population	Section 6

14.3.1.2	Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Severity – Safety Population	Section 6
14.3.1.3	Treatment Emergent Treatment-Related Adverse Events by System Organ Class and Preferred Term – Safety Population	Table 14.3.1.1
14.3.1.4	Treatment Emergent Treatment-Related Adverse Events by System Organ Class, Preferred Term and Severity – Safety Population	Table 14.3.1.2

Listing No.	**Listing Title (including population)**	**Template**
14.3.2.1	Deaths – All Randomized Subjects	16.2.7.1
14.3.2.2	Serious Adverse Events leading to Discontinuation – All Randomized Subjects	16.2.7.1
16.1.7	Randomization information – All Randomized Subjects	Appendix 8
16.2.1.1	Subject Disposition – All Screened Subjects	Appendix 8
16.2.2	Individual Subjects Protocol Violation – All Randomized Subjects	Appendix 8
16.2.3.1	Exclusions from Analysis Populations – All Randomized Subjects	Appendix 8
16.2.4.1	Demographic Characteristics – All Randomized Subjects	Appendix 8
16.2.4.2	Medical History – All Randomized Subjects	Appendix 8
16.2.6.1	Dermatologist and Ophthalmologist Scores – All Randomized Subjects	Appendix 8
16.2.6.2.1	Subject Self-Assessment (Face) – All Randomized Subjects	Appendix 8
16.2.6.2.2	Subject Self-Assessment (Eye) – All Randomized Subjects	Appendix 8
16.2.7.1	All Adverse Events – All Randomized Subjects	Appendix 8
16.2.7.2	All Adverse Events – Non Randomized Subjects	16.2.7.1

8 Template for Tables, Figures and Listings

Protocol: 207782 Program Run Date: ddmonyyyy

Table 14.1.1
Subject Disposition

	Micellar Cleanser N (%)	Micellar Foaming Cleanser N (%)	Overall N (%)
TOTAL SUBJECTS SCREENED			XX
SUBJECTS NOT RANDOMISED			XX
DID NOT MEET STUDY CRITERIA			XX (XX.XX)
ADVERSE EVENT			XX (XX.XX)
LOST TO FOLLOW - UP			XX (XX.XX)
PROTOCOL VIOLATION			XX (XX.XX)
WITHDRAWAL OF CONSENT			XX (XX.XX)
OTHER			XX (XX.XX)
SUBJECTS RANDOMISED	XX	XX	XX
COMPLETED STUDY	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
DID NOT COMPLETE STUDY	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
DID NOT MEET STUDY CRITERIA	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
ADVERSE EVENT	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
LOST TO FOLLOW - UP	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
PROTOCOL VIOLATION	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
WITHDRAWAL OF CONSENT	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
OTHER	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
SAFETY POPULATION	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
ITT POPULATION	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
PP POPULATION	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)

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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.

Protocol: 207782 Program Run Date: ddmonyyyy

Table 14.1.2
Demographic Characteristics
Safety Population

Study Population: Safety (N=xxx)

	Micellar Cleanser (N=xx)	Micellar Foaming Cleanser (N=xx)	Overall (N=xx)
SEX n (%)			
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 – JAPANESE HERITAGE			
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)
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
CONTACT LENS WEARER			
YES	XX (XX.X)	XX (XX.X)	XX (XX.X)
NO	XX (XX.X)	XX (XX.X)	XX (XX.X)
FITZPATRICK SKIN TYPE n (%)			
I	XX (XX.X)	XX (XX.X)	XX (XX.X)
II	XX (XX.X)	XX (XX.X)	XX (XX.X)
III	XX (XX.X)	XX (XX.X)	XX (XX.X)
IV	XX (XX.X)	XX (XX.X)	XX (XX.X)
V	XX (XX.X)	XX (XX.X)	XX (XX.X)

VI	XX (XX.X)	XX (XX.X)	XX (XX.X)
COSMETIC SKIN TYPE n (%)			
DRY	XX (XX.X)	XX (XX.X)	XX (XX.X)
NORMAL/COMBINATION	XX (XX.X)	XX (XX.X)	XX (XX.X)

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Protocol: 207782 Program Run Date: ddmonyyyy

Table 14.2.1.1
Frequency of Combined Dermatologist and Ophthalmologist Score
Intent to Treat Population

Intent to Treat Population (N=XX)

Timepoint Combined Dermatologist and Ophthalmologist Score	Micellar Cleanser (N=XX) n (%)	Micellar Foaming Cleanser (N=XX) n (%)
BASELINE		
0	xx (xx.xx)	xx (xx.xx)
1	xx (xx.xx)	xx (xx.xx)
2	xx (xx.xx)	xx (xx.xx)
….	xx (xx.xx)	xx (xx.xx)
16	xx (xx.xx)	xx (xx.xx)
1 HOUR		
0	xx (xx.xx)	xx (xx.xx)
1	xx (xx.xx)	xx (xx.xx)
2	xx (xx.xx)	xx (xx.xx)
….	xx (xx.xx)	xx (xx.xx)
16	xx (xx.xx)	xx (xx.xx)
DAY 21#		
0	xx (xx.xx)	xx (xx.xx)
1	xx (xx.xx)	xx (xx.xx)
2	xx (xx.xx)	xx (xx.xx)
….	xx (xx.xx)	xx (xx.xx)
16	xx (xx.xx)	xx (xx.xx)
SUM OF POST-BASELINE COMBINED DERMATOLOGIST AND OPHTHALMOLOGIST SCORES		
0	xx (xx.xx)	xx (xx.xx)
1	xx (xx.xx)	xx (xx.xx)
2	xx (xx.xx)	xx (xx.xx)
….	xx (xx.xx)	xx (xx.xx)
32	xx (xx.xx)	xx (xx.xx)

Combined dermatologist and ophthalmologist score = dermal response score + superficial irritation score + conjunctive involvement score + lacrimal intensity score

Primary endpoint is at Day 21.

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Programming Note:

- This shell is used for tables 14.2.1.2, 14.2.2.1, 14.2.2.2, 14.2.4.1, 14.2.4.2 14.2.7.1 and 14.2.7.2. Replace the formula in the footnote with the correct applicable formula. For the tables by strata add “Strata: NOT contact lens wearer with Dry skin” etc. below the line “Intent to Treat Population (N=XX)”. Remove # footnote for all other tables.

Protocol: 207782 Program Run Date: ddmonyyyy

Table 14.2.5.1
Frequency of Dermal Response Score
Intent to Treat Population

Intent to Treat Population (N=XX)

Timepoint Dermal Response Score	Micellar Cleanser (N=XX) n (%)	Micellar Foaming Cleanser (N=XX) n (%)
BASELINE		
0	xx (xx.xx)	xx (xx.xx)
1	xx (xx.xx)	xx (xx.xx)
2	xx (xx.xx)	xx (xx.xx)
….	xx (xx.xx)	xx (xx.xx)
7	xx (xx.xx)	xx (xx.xx)
1 HOUR		
0	xx (xx.xx)	xx
1	xx (xx.xx)	xx
2	xx (xx.xx)	xx
….	xx (xx.xx)	xx
7	xx (xx.xx)	xx
DAY 21		
0	xx (xx.xx)	xx (xx.xx)
1	xx (xx.xx)	xx (xx.xx)
2	xx (xx.xx)	xx (xx.xx)
….	xx (xx.xx)	xx (xx.xx)
SUM OF POST-BASELINE DERMAL RESPONSE SCORES		
……	xx (xx.xx)	xx (xx.xx)

0 = No evidence of irritation; 1= Minimal erythema barely perceptible; 2 = Definite erythema; readily visible;or minimal edema; minimal popular response; 3 = Erythema and papules;4 = Definite edema; 5 = Erythema, edema and papules; 6 = Vesicular eruption; 7 = Strong reaction spreading beyond test site.

Programming Note:

- This shell is used for tables 14.2.3.2, 14.2.6.1 and 14.2.6.2. Replace the score decode footnote with the corresponding footnote. For the tables by strata add "Strata: NOT contact lens wearer with Dry skin" etc. below the line "Intent to Treat Population (N=XX)".

Protocol: 207782 Program Run Date:ddmonyyyy

Table 14.2.6.1
Frequency of Conjunctiva Involvement Score
Intent to Treat Population

Intent to Treat Population (N=XX)

Timepoint Conjunctiva Involvement Score/Grade	Micellar Cleanser (N=XX) n (%)	Micellar Foaming Cleanser (N=XX) n (%)
BASELINE		
0/NONE	xx (xx.xx)	xx (xx.xx)
1/MILD	xx (xx.xx)	xx (xx.xx)
2/MODERATE	xx (xx.xx)	xx (xx.xx)
3/SEVERE	xx (xx.xx)	xx (xx.xx)
1 HOUR		
0/NONE	xx (xx.xx)	xx (xx.xx)
1/MILD	xx (xx.xx)	xx (xx.xx)
2/MODERATE	xx (xx.xx)	xx (xx.xx)
3/SEVERE	xx (xx.xx)	xx (xx.xx)
DAY 21		
0/NONE	xx (xx.xx)	xx (xx.xx)
1/MILD	xx (xx.xx)	xx (xx.xx)
2/MODERATE	xx (xx.xx)	xx (xx.xx)
3/SEVERE	xx (xx.xx)	xx (xx.xx)
SUM OF POST-BASELINE CONJUNCTIVA INVOLVEMENT SCORES		
……	xx (xx.xx)	xx (xx.xx)

None = No involvement; Mild = Conjunctivae (palpebral and bulbar) injected above normal with possible chemosis (swelling); no discharge; Moderate = Conjunctivae injected above normal; obvious swelling; possible discharge; Severe = Conjunctivae more diffuse, deeper crimson red, individual vessels not easily discernible; excessive swelling and/or discharge

PPD

Programming Note:

- This table shell is used for Table 14.2.5.2 as well. Add “Strata: NOT contact lens wearer with Dry skin” etc. below the line “Intent to Treat Population (N=XX)”.

Protocol: 207782 Program Run Date:ddmonyyyy

Table 14.2.8.1
Frequency of Subject Assessment Scores for Eyes
Intent to Treat Population

Intent to Treat Population (N=XX)

Assessment: Redness

Timepoint	Micellar Cleanser (N=XX) n (%)	Micellar Foaming Cleanser (N=XX) n (%)
BASELINE		
0/NONE	xx (xx.xx)	xx (xx.xx)
1/MILD	xx (xx.xx)	xx (xx.xx)
2/MODERATE	xx (xx.xx)	xx (xx.xx)
3/SEVERE	xx (xx.xx)	xx (xx.xx)
1 HOUR		
0/NONE	xx (xx.xx)	xx (xx.xx)
1/MILD	xx (xx.xx)	xx (xx.xx)
2/MODERATE	xx (xx.xx)	xx (xx.xx)
3/SEVERE	xx (xx.xx)	xx (xx.xx)
DAY 21		
0/NONE	xx (xx.xx)	xx (xx.xx)
1/MILD	xx (xx.xx)	xx (xx.xx)
2/MODERATE	xx (xx.xx)	xx (xx.xx)
3/SEVERE	xx (xx.xx)	xx (xx.xx)
SUM OF POST-BASELINE REDNESS SCORES		
.....	xx (xx.xx)	xx (xx.xx)

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PPD

Programming Note: Repeat for Dryness, Burning, Itching and Stinging. This shell will also be used for table 14.2.9.1.

Protocol: 207782 Program Run Date:ddmonyyyy

Table 14.2.8.2
Frequency of Subject Assessment Combined Score* for Eyes
Intent to Treat Population

Intent to Treat Population (N=XX)

Timepoint	Micellar Cleanser (N=XX) n (%)	Micellar Foaming Cleanser (N=XX) n (%)
BASELINE		
0	xx (xx.xx)	xx (xx.xx)
1	xx (xx.xx)	xx (xx.xx)
…	xx (xx.xx)	xx (xx.xx)
15	xx (xx.xx)	xx (xx.xx)
1 HOUR		
0	xx (xx.xx)	xx (xx.xx)
1	xx (xx.xx)	xx (xx.xx)
…	xx (xx.xx)	xx (xx.xx)
15	xx (xx.xx)	xx (xx.xx)
DAY 21		
0	xx (xx.xx)	xx (xx.xx)
1	xx (xx.xx)	xx (xx.xx)
…	xx (xx.xx)	xx (xx.xx)
15	xx (xx.xx)	xx (xx.xx)
SUM OF POST-BASELINE COMBINED SCORE* FOR EYES		
……	xx (xx.xx)	xx (xx.xx)

* Combined score for eyes is obtained by summing the 5 subject assessments for eyes i.e. redness, dryness, burning, itching and stinging.

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Programming Note:This shell will also be used for table 14.2.9.2 (same footnote applies).

Protocol: 207782 Program Run Date: ddmmmyyyy

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

System Organ Class Preferred Term	Micellar Cleanser (N=xx)		Micellar Foaming Cleanser (N=xx)		Overall (N=xx)	
	n (%)	nAE	n (%)	nAE	n (%)	nAE
NUMBER OF SUBJECTS WITH AT LEAST ONE AE	xx (xx.x)		xx (xx.x)		xx (xx.x)	
NUMBER OF SUBJECTS WITH NO AE	xx (xx.x)		xx (xx.x)		xx (xx.x)	
AUTONOMIC NERVOUS SYSTEM	x (x.x)	x	x	x	x	x
MOUTH DRY	x (x.x)	x	x	x	x	x
BODY AS A WHOLE GENERAL	x (x.x)	x	x	x	x	x
PAIN	x (x.x)	x	x	x	x	x
CENTRAL AND PERIPHERAL NERVOUS SYSTEM	x (x.x)	x	x (x.x)	x	x (x.x)	x
DIZZINESS	x	x	x (x.x)	x	x	x
HEADACHE	x (x.x)	x	x	x	x (x.x)	x
GASTROINTESTINAL SYSTEM	x	x	x	x	x (x.x)	x
ABDOMINAL PAIN	x	x	x	x	x	x
ANOREXIA	x	x	x	x	x (x.x)	x
VOMITING	x	x	x	x	x	x

n (%) = Number (percent) of subjects. nAE = Number of Adverse Events.

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Protocol: 207782 Program Run Date: ddmmmyyyy

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

	Micellar Cleanser (N = XX)			Micellar Foaming Cleanser (N = XX)		
	n (%) nAE			n (%) nAE		
System Organ Class Preferred Term	Mild	Moderate	Severe	Mild	Moderate	Severe
Any 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
Nervous system 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
Headache	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
Dizziness	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
Respiratory, thoracic and mediastinal 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
Nasal mucosal erosion	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
Nasal congestion	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
Nasal discomfort	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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Listing 16.1.7
Randomization Information
All Randomized Subjects

Study Population: Randomised Subjects (N=xxx)
Stratum: Not contact lens wearer with dry skin

Subject	Randomisation Number	Treatment	Randomisation Date
PPD		MICELLAR CLEANSER	DDMMYYYY
		MICELLAR FOAMING CLEANSER	DDMMYYYY

…

PPD

Protocol: 207782 Program Run Date: DDMMMYYYY

Listing 16.2.1.1
Subject Disposition
All Screened Subjects

Subject	Sex/Age/ Race [1]	Screening date	Treatment Start Date and Time	Date of Completion or withdrawal	Duration of Treatment (Days)	Completed (Yes/No)	Randomized (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.

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PPD

Protocol: 207782 Program Run Date: DDMMMYYYY

Listing 16.2.2
Individual Subjects Protocol Violation
All Randomised Subjects

Treatment Group: Micellar Cleanser

Subject	Age/Sex/Race[1]	Visit	Violation Sequence	Protocol Violation
PPD				xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

[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.

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PPD

Protocol: 207782 Program Run Date: DDMMMYYYY

Listing 16.2.3.1
Exclusions from Analysis Populations
All Randomized Subjects

Treatment Group: Micellar Cleanser

Subject	Sex/Age/ Race [1]	Treatment Start Date and Time	Safety (Yes/No)	Intent To Treat (Yes/No)
PPD			No	No
….				

[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: 207782 Program Run Date: DDMMMYYYY

Listing 16.2.4.1
Demographic Characteristics
All Randomized Subjects

Treatment Group: Micellar Cleanser

Subject	Sex	Race	Age (years)	Contact Lens Wearer (Yes/No)	Fitzpatrick Skin Type	Cosmetic Skin Type
PPD						
….						

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PPD

Protocol: 207782 Program Run Date: DDMMMYYYY

Listing 16.2.4.2
Medical History
All Randomized Subjects

Treatment Group: Micellar Cleanser

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

….

[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: 207782 Program Run Date: DDMMMYYYY

Listing 16.2.6.1
Dermatologist and Ophthalmologist Scores
All Randomized Subjects

Treatment Group: Micellar Cleanser

Subject	Sex/Age/ Race [1]	Visit	Visit Date	Dermal Response Score [2]	Superficial Irritation Score [3]	Combined Dermatologist Score	Conjunctiva Involvement (Score) [4]	Lacrimal Intensity (Score) [5]	Combined Ophthalmologist Score	Combined Dermatologist and Ophthalmologist Score	Combined Dermatologist and Ophthalmologist Score (modified)
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] 0 = No evidence of irritation; 1 = Minimal erythema; barely perceptible; 2 = Definite erythema, readily visible or minimal edema or minimal popular response; 3 = Erythema and papules; 4 = Definite edema; 5 = Erythema, edema and papules; 6 = Vesicular eruption; 7 = Strong reaction spreading beyond test site.
[3] A(0) = Slight glazed appearance; B(1) = Marked glazing; C(2) = Glazing with peeling and cracking; F(3) Glazing and fissures; G(3) = Film of dried serous exudate covering all or portion of the patch; H(3) = Small petechial erosions and/or scabs.
[4] 0 = None – No involvement; 1 = Mild – Conjunctivae (palpebral and bulbar) injected above normal with possible chemosis (swelling), no discharge; 2 = Moderate – Conjunctivae injected above normal, obvious swelling, possible discharge; 3 = Severe – Conjunctivae more diffuse, deeper crimson red, individual vessels not easily discernible, excessive swelling and/or discharge.
[5] 0 = None – No lacrimal observation; 1 = Mild – Excessive wetness (no distinct tears); 2 = Moderate – A few formed tears (contained in orbit); 3 = Severe – Intense tearing (leaving orbit).
Combined Dermatologist and Ophthalmologist Score = Combined Dermatologist Score + Combined Ophthalmologist Score.
Combined Dermatologist and Ophthalmologist Score (modified) = Dermal Response Score + Conjunctiva Involvement Score + Lacrimal Intensity Score.

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Programming Note: Please include the sum of post baseline scores.

Protocol: 207782 Program Run Date: DDMMMYYYY

Listing 16.2.6.2.1
Subject Self-Assessment (Face)
All Randomised Subjects

Treatment Group: Micellar Cleanser

Subject	Sex/Age/ Race [1]	Visit	Visit Date	Redness	Dryness	Burning	Itching	Stinging	Combined Score
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

Programming Note: Please include the sum of post baseline scores.

Protocol: 207782 Program Run Date: DDMMMYYYY

Listing 16.2.6.2.2
Subject Self-Assessment (Eye)
All Randomised Subjects

Treatment Group: Micellar Cleanser

Subject	Sex/Age/ Race [1]	Visit	Visit Date	Redness	Dryness	Burning	Itching	Stinging	Combined Score
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

Programming Note: Please include the sum of post baseline scores.

Protocol: 207782 Program Run Date: DDMMMYYYY

Listing 16.2.7.1
All Adverse Events

All Randomized Subjects

Treatment Group: Micellar Cleanser

Subject	Sex/Age/ 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, M = 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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Programming Note:

- Repeat the same layout for the 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.

inVentiv Health	**Client Approval Form: Final Statistical Analysis Plan Text and Shells**

Project Identifiers	
Client: GSKCH	Protocol No.: 207782
Project ID Code: CCI	Protocol Version (date) (DD-MMM-YYYY): 16-Aug-2017
SAP Version: 2.0	SAP Author: PPD
SAP Date (DD-MMM-YYYY): 16-Aug-2017	

The signatures below acknowledge that the Statistical Analysis Plan Text and Shells prepared by inVentiv Health for GSKCH are final.

Approved by: <client>	PPD PRINTED NAME	PRINCIPAL STATISTICIAN TITLE
	PPD SIGNATURE	PPD DATE OF SIGNATURE (DDMMMYYYY)
Approved by: Lead Statistician, inVentiv Health	PPD PRINTED NAME	MANAGER, BIOSTATISTICS TITLE
	PPD SIGNATURE	PPD DATE OF SIGNATURE (DDMMMYYYY)

STATISTICAL REPORTING AND ANALYSIS PLAN
Addendum 1

A Clinical Study to Assess the Cutaneous and Ocular Local Tolerance of Two Cosmetic Facial Cleansers in Healthy Females with Sensitive Skin Under Normal Conditions of Use

Protocol Number: 207782

Phase: N/A

Document History

Document	Version Date	Summary of Changes (New analysis or Change in planned analysis)
Addendum 1	04-Dec-2017	Disposition table includes additional summary for total number of subjects who underwent the lactic acid sting test. Change in the definition of Safety Population Added TEAEs definition for more clarity.
Amendment 1	14-Aug-2017	Added new mandatory listings and incorporated in new template.
Original Analysis Plan	30-Jun-2017	Not applicable (N/A)

Table of contents

1 Introduction

This RAP addendum describes the changes, deviations and clarifications to the planned analysis described in the Statistical Reporting and Analysis Plan Amendment 1 and protocol version 2.0. These changes were identified during CSR development, and hence were identified after unblinding but prior to final CSR. These changes will be reflected in the final CSR.

The sections below provide the updated text that are required from the planned analysis, with section 5.0 providing further details on what was planned, the change and the reason for the change. A summary of the changes/clarifications are:

- Number of subjects who underwent the lactic acid sting test: this summary will be added to the disposition table 14.1.1.
- Safety population definition: The definition applied to the tables, figures and listings (TFLs) differed from the planned definition in the RAP amendment and protocol V2.0.
- Treatment emergent adverse event (TEAE) definition: No definition was previously provided; hence a definition has been added for clarity and consistency with the updated safety population definition.
- Update to study duration derivation in Listing 16.2.1.1

4.1 Populations for Analysis

4.1.1 Subject Disposition

Screen failures will be defined as subjects who do not satisfy all the inclusion/exclusion criteria. A summary will be provided of the number of subjects screened and the number of screen failures with reasons why subjects were not randomized. Additionally, the number and percentage of subjects who underwent the lactic acid sting test will also be presented (Table 14.1.1).

Subject disposition will also be summarized 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 summarize the number and percent of subjects assigned to each analysis population (refer to section 4.1.3).

Subject disposition including the subject status (completer, Yes/No), critical demographic data (age, sex, race), the duration of treatment [(date of completion or withdrawal - treatment start date)+1] before discontinuation and the specific reason for discontinuation, will be listed in Listing 16.2.1.1. by treatment group.

4.1.3 Analysis Populations

Two analysis populations are defined.

Population	Definition / Criteria	Analyses Evaluated
Safety	• All subjects, for whom the lactic acid stinging test was performed, were randomized and had at least one study treatment application. • This population will be based on the treatment the subject actually received.	• Safety
Intent-To-Treat	• Comprises of all randomized subjects who have at least one cutaneous or ocular assessment following study product application. • This population will be based on the treatment the subject is randomised to.	• Efficacy

4.6 Analysis of Safety

4.6.1 Adverse Events and Serious Adverse Events

Adverse events (AEs) will be captured following the lactic acid stinging test procedure.

All adverse events (AEs) will be summarised by primary system organ class and preferred term according to the current version of the MedDRA.

TEAEs are defined as new AEs that occur on or after the date/time of first supervised treatment product use. Events with an onset date/time prior to the first use of treatment product will be considered as non-treatment emergent.

Treatment emergent adverse events (TEAEs) will be summarized by the number and percentage of subjects having any adverse event, an adverse event in each System Organ Class, and each individual adverse event. All TEAEs will also be tabulated by severity. Treatment-emergent AEs suspected of a relationship to study product will be presented in a similar manner. For treatment-related AEs, these will also be presented by severity.

Deaths occurring during treatment (if any) will be listed by treatment, including the date and study day of death, and the principal cause of death. Serious adverse events leading to discontinuation will be listed. All AEs will be listed.

5 Changes to the Statistical Analysis Plan

Any changes from the originally planned statistical analysis specified in the SAP amendment (dated 16-AUG-2017) are outlined in Table 1.

Table 1 Changes to SAP amendment Defined Analysis Plan

SAP Analysis Plan Amendment 1	Statistical Analysis Plan Addendum	Rationale for Changes
• 1.1.2 Analysis Population The Safety population includes all subjects from the point of the lactic acid stinging test procedure until completion of the study.	• 1.1.2 Analysis Population All subjects, for whom the lactic acid stinging test was performed, were randomized and had at least one study treatment application.	It was originally planned to report all AEs from the point of lactic acid sting test as the subjects would have been applied the acid solution to potential subjects in the study. However this sting test was performed at the screening visit and therefore not everyone who had the sting test performed would have been randomised and received treatment product. Therefore some of the AEs reported after the sting test would not have been classified as treatment emergent. During the programming of the AE TFLs for the CSR, it was assumed all subjects in safety population were randomized and received treatment product, hence any AEs from this safety population definition would have been TEAEs (if started after product use). However the safety population definition applied to the TFLs differed from the planned definition. Once this was identified during the CSR development, the study team decided that the definition of the safety population and TEAE definition applied to the TFLs was the most appropriate. Hence change/clarification to the definitions in this RAP addendum.
• Section 4.1.1 Subject Disposition	• Section 4.1.1 Subject Disposition Additional summary of the number and percentage of subjects who underwent the lactic acid sting test (Table 14.1.1).	This information will be useful in the CSR to assess the disposition of subjects between onset of screening and randomisation.
	• The derivation for treatment duration has been added in the listing shell in Section 7 as well as in the text under section 4.1.1.	• While reviewing the draft CSR, it had been identified that the calculation of the treatment duration in Listing 16.2.1.1 was not correct (addition of 1 day was not added). No derivation had previously been provided in the RAP amendment.

7 Template for Table and Listing

Protocol: 207782 Program Run Date: ddmonyyyy

Table 14.1.1
Subject Disposition

All Screened Subject (N=XXX)

	Micellar Cleanser N (%)	Micellar Foaming Cleanser N (%)	Overall N (%)
TOTAL SUBJECTS SCREENED			XX
TOTAL SUBJECTS UNDERWENT LACTIC ACID STING TEST			XX (XX.XX)
SUBJECTS NOT RANDOMISED			XX
DID NOT MEET STUDY CRITERIA			XX (XX.XX)
ADVERSE EVENT			XX (XX.XX)
LOST TO FOLLOW - UP			XX (XX.XX)
PROTOCOL VIOLATION			XX (XX.XX)
WITHDRAWAL OF CONSENT			XX (XX.XX)
OTHER			XX (XX.XX)
SUBJECTS RANDOMISED	XX	XX	XX
COMPLETED STUDY	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
DID NOT COMPLETE STUDY	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
DID NOT MEET STUDY CRITERIA	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
ADVERSE EVENT	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
LOST TO FOLLOW - UP	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
PROTOCOL VIOLATION	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
WITHDRAWAL OF CONSENT	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
OTHER	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
SAFETY POPULATION	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
ITT POPULATION	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)

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

Protocol: 207782 Program Run Date: DDMMMYYYY

Listing 16.2.1.1
Subject Disposition
All Screened Subjects

Subject	Sex/Age/ Race [1]	Screening date	Treatment Start Date and Time	Date of Completion or withdrawal	Duration of Treatment (Days) [2]	Completed (Yes/No)	Randomized (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.
[2] Treatment duration is calculated as [(date of completion or withdrawal minus treatment start date) +1].

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inVentiv Health	Client Approval Form: Final Statistical Reporting and Analysis Plan Shells Addendum

Project Identifiers	
Client: GSKCH	Protocol No.: 207782
Project ID Code: CCI	Protocol Version (date): 2.0 (26-May-2017)
RAP Version: Addendum 1	RAP Author: PPD
RAP Date : 07-Dec-2017	

The signatures below acknowledge that the Statistical Reporting and Analysis Plan Shells addendum prepared by inVentiv Health for GSKCH are final.

Approved by: GSKCH	PPD	PRINCIPAL STATISTICIAN
	PRINTED NAME	TITLE
	PPD	PPD
	SIGNATURE	DATE OF SIGNATURE (DDMMMYYYY)
Approved by: Lead Statistician, inVentiv Health	PPD	STATISTICIAN II
	PRINTED NAME	TITLE
	PPD	PPD
	SIGNATURE	DATE OF SIGNATURE (DDMMMYYYY)