CONFIDENTIAL

STATISTICAL ANALYSIS PLAN FOR PROTOCOL 207587

A Clinical Study to Assess the Photosensitisation and Photoallergy Potential of a Cosmetic Facial Product in Healthy Subjects

BIOSTATISTICS DEPARTMENT

GLAXOSMITHKLINE CONSUMER HEALTHCARE

Document type:	Statistical Analysis Plan
Authors:	PPD (statistician II) inVentiv Health
Document status:	Final 1.0
Release date:	11-MAY-2017

The purpose of this Statistical Analysis Plan (SAP) is to describe the planned analyses and output to be included in the Clinical Study Report (CSR) for Protocol 207587. The SAP will be finalized prior to data base freeze and treatment code un-blinding.

1 Study details

A cosmetic product that is freely available to the consumer must be safe when applied under normal or reasonably foreseeable conditions of use. As a general requirement, the safety and compatibility of a new formulation should be confirmed before it is commercialised. (Guideline for the Safety Evaluation of Cosmetic Products; Agencia Nacional de Vigilancia Sanitaria, ANVISA, 2012).

Compatibility studies, performed as patch tests, aim to confirm the local tolerance of topical cosmetic products during the first application to the skin, therefore providing assurance that the product is safe for use under maximized conditions (ANVISA, 2012).

Phototoxicity assessments aim to demonstrate the absence of irritation potential of a product when applied to the skin and exposed to ultra violet (UVA) radiation. Photosensitisation assessments aim to prove the absence of allergic potential of a product applied to the skin when exposed to UVA radiation.

In this three-phase phototoxicity-photosensitisation (PT-PA) study, the test material and a positive control of saline solution are applied under a semi-occlusive patch to the upper back of each subject. The first phase of the study is an Induction Phase; a controlled amount of the test product and control product is applied over a defined surface area of skin (amount per unit area), under a semi-occlusive patch. The patch will remain on the skin for 24 (±2) hours during this phase. Following patch removal the patch site will be exposed to ultraviolet – A (UVA) radiation and re-assessed 48 hours later prior to re-application of another semi-occlusive patch (with both the test and control product) to the same site. The Induction phase will last 3 weeks. After a subject completes the Induction Phase they will enter a Rest Phase of 2 weeks duration, during which no patches will be applied. After the Rest Phase, subjects will return to the clinical site for the Challenge Phase. In the Challenge phase two test patches will be applied to virgin skin areas on each subjects' upper back for 24 hours. Following removal of both patches, one of the Challenge patch test sites will be exposed to UVA radiation. Both Challenge patch test sites will be assessed up until 72 (±2) hours later.

The objective of this clinical study is to assess the phototoxicity and photosensitisation potential of a cosmetic test product under exaggerated conditions of use with controlled product application and under supervision of a dermatologist.

1.1 Study design

Overall Design
This is an assessor-blinded (single), test site randomised, intra-subject comparison, repeated insult patch test to evaluate the skin irritation and sensitisation potential of a cosmetic facial product, under exaggerated conditions of use with controlled product application and under supervision of a dermatologist.
Day -14 to 0 / Visit 1 - Screening Visit **NOTE: Visit 1 and Visit 2 could be combined**

The following assessments will be conducted: 1. Subject Informed Consent taken 2. Subject demographics collected 3. Medical history details 4. Details of current and concomitant medication collected 5. Fitzpatrick Skin Type Assessment (Appendix 3 of the protocol) 6. Inclusion/Exclusion criteria 7. Dermatologist determination for eligibility to participate in the stud (including visual examination of the dorsum scapular region) 8. Subject Eligibility
Day 1 to 22/ Visit 2 – Visit 14 – Induction Phase (3 Weeks) **NOTE: Visit 1 and Visit 2 could be combined**
The following assessments will be conducted: 1. Continued eligibility check 2. Current/Concomitant Medications review 3. Inclusion/Exclusion criteria review (Inclusion criteria 3c (only) at Visit 2 as per protocol, if Visit 1 and 2 are not combined). 4. Dermatologist determination for continued eligibility to participate in the study (Visit 2/ Day 1 only - if visits not combined) 5. Test Site Designation and Randomisation (Visit 2/Day 1 only). 6. Baseline grading/assessment of test sites (Per Appendix 2 of the protocol) (Visit 2/Day 1 only) 7. Patch applications (9 patch applications to the same test site, over 3 consecutive weeks with patches applied on alternate weekdays). 8. Patch removal 24 (± 2) hours after application (Tuesday and Friday). Reaction grading/assessment performed by a qualified staff member (24 ±2 hours after application). Grading/assessments will be 30 minutes (up to 1 hour) after each patch removal (per Appendix 2 of the protocol) 9. Application site exposed to UVA irradiation. 10. 48 (± 2) hours after each UVA irradiation (or 72 (± 2) hours, in case of irradiation on Fridays), the sites will be evaluated for signs of dermatological reactions, according to Appendix 2 of the protocol. 11. Adverse event assessment *NOTE: Subjects will report to the study site 12 times during the Induction Phase (6 patch applications and removals) and once for final Induction Phase patch grading/assessment on the first day of the rest phase (Visit 14/Day 22). No Patch Applications from Days 22 to 35 (Rest Phase).*
Day 22 – Day 35/ Visit 14 – Rest Phase (2 Weeks) **No Patch Application**
Days 36 to 39 / Visit 15 to Visit 18 - Challenge Phase
The following assessments will be conducted: 1. Continued eligibility check 2. Current/Concomitant Medications review

3. Grading/assessment of naïve challenge patch site performed by a qualified staff member. (As per Appendix 2 of the Protocol). Prior to Challenge patch application. (Visit 15/Day 36). 4. Challenge Patch application, 2 patches to naïve sites (Visit 15/Day 36). 5. Patch removal 24 (± 2) hours later (Visit 16/Day 37). 6. Reaction grading/assessment performed by a qualified staff member at approximately 30 minutes (maximum 1 hour) after patch removal (Visit 16/Day 37). 7. One of the naïve patched sites will be exposed to 5 Joules per square centimeter (J /cm2) UVA radiation. 8. Subjects will return for grading/assessment performed by a qualified staff member 24 (± 2) hours after UVA irradiation (Visit 17/Day 38). Both irradiated non non-irradiated sites will be assessed. 9. Subjects will return for grading/assessment performed by a qualified staff member 48 (± 2) hours after UVA irradiation (Visit 18/Day 39). Both irradiated non non-irradiated sites will be assessed. 10. Adverse event assessment.
Day 40 / Visit 19 – End of Study
The following assessments will be conducted: 1. Current/Concomitant Medications review 2. Adverse event assessment. 3. Subjects will return for grading/assessment performed by a qualified staff member 72 (± 2) hours after UVA irradiation (Visit 19/Day 40). Both irradiated and non-irradiated sites will be assessed. 4. Dermatologist final assessment. 5. Subject discharge from the study site following completion of all study procedures.

1.2 Study objectives

Objectives	Endpoints
Primary Objective	**Primary Endpoint**
To determine the photoirritation and photosensitisation potential of a cosmetic facial skin product after repeated patch applications to the skin of healthy subjects.	Trained assessor assessment of local tolerance through visual assessment of cutaneous irritation via the combined dermal response and other effects scores over the induction and challenge phase.
Secondary Objectives	**Secondary Endpoint**
To evaluate the general safety of a cosmetic facial skin product.	Assessment of frequency and severity of Adverse Events (AEs)

1.3 Treatments

	Test Product	Reference Product
Product Name	Facial micellar cleanser	Saline Solution: Sodium chloride (NaCl; 0.9%)
Product Formulation Code (MFC)	CCI [redacted]	N/A Site to supply
Product Format	200 ml clear PET Bottle	N/A
Application Quantity	0.02 millilitres/square centimetre (ml/cm^2)	0.02 ml/cm^2
Route of Administration	Topical dermal application via semi occlusive patch	
Application Instruction	Applied on-site by technician	

During the induction phase, there will be 6 patch applications (a patch will contain both the test product and saline solution) over 3 consecutive weeks, with each patch applied on Mondays and Thursdays. Each patch will remain in place for 24 (± 2) hours and then be removed, the treated areas will be cleaned with saline solution. After 30 minutes (maximum of 1 hour) the sites will be graded/evaluated as per the scale in Appendix 2 of the protocol. The patch test site will then be exposed to 5 J/cm^2 UVA radiation. The patch application site will be assessed pre-irradiation, following patch removal. Irradiation time depends on the power output of the light source and distance from the subject, and will be determined by the study site prior to UVA exposure. Irradiation will occur on the same days as patch removal (Tuesday and Fridays). Assessment of the irradiated sites will occur 48 hours (or 72 hours if the irradiation occurred on a Friday) after UVA exposure, prior to new patch application to the same site.

After the last grading/evaluation of the Induction Phase, subjects will enter a Rest Phase of 2 weeks. During this time there will be no product patch applications.

After completing the Rest Phase, subjects will return for the Challenge Phase. Two naïve sites (previously un-patched, virgin areas) will be selected for the challenge patches both of these naïve areas will be graded/evaluated prior to any product application. Two patches, each with the test product and saline solution, will be randomly applied to each of the Challenge sites for 24 (± 2) hours, according to each subject's random assignment on Day 1 of the Induction phase. After 24 (± 2) hours, subjects will return for Challenge patch removal, the sites will be cleaned with saline solution and then graded/evaluated after 30 minutes (maximum of 1 hour). One of the Challenge patch sites will then be irradiated with 5 J/cm2 of UVA radiation. Subjects will return 24 (± 2), 48 (± 2), and 72 (± 2) hours after patch removal for further grading/assessments of both the irradiated and non-irradiated Challenge sites.

After the Challenge Phase is complete, a final clinical assessment by a qualified dermatologist will be performed to ensure that it is medically appropriate to exit each subjects from the study. After all study assessments are completed, subjects will be discharged from the study site.

1.4 Time points and visit windows

All data will be accepted for the analysis. Deviations from the scheduled assessment times are expected to be small and few. The following are the acceptable time windows.

Phase	Activity	Time window
Induction Phase	Patches application	Monday and Thursday for 3 consecutive weeks
	Patches removal	24 (±2) hours Tuesday and Friday
	Patches applied on Friday will remain in place	72 (± 2) hours until Monday
	Assessment after patch removal	30 minutes (up to 1 hour)
	UVA irradiation evaluation	48 (±2) hours after each irradiation 72 (±2) hours in case on Fridays
Challenge phase	Patches will remain in place	24 (± 2) hours during the week
	Assessment after patch removal	30 minutes (up to 1 hour)
	Further assessment after patch removal	24 (± 2), 48 (± 2) and 72 (± 2) hours
	UVA irradiation evaluation	48 (±2) hours after each irradiation

2 Data analysis

Data analysis will be performed by inVentiv Health Clinical. Prior to database hard lock 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.

2.1 Populations for analysis

2.1.1 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 randomised.

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 2.1.3).

2.1.2 Protocol Deviations

Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, patient management or patient assessment) will be listed.

Protocol violations deviations will be tracked by the study team throughout the conduct of the study. Data will be reviewed prior to un-blinding and hard lock of the database to ensure all important deviations are captured and categorised.

The important protocol deviations may occur for the following reasons; however, the reasons are not limited and exhaustive.

- Deviation of inclusion or exclusion criteria at screening that may affect efficacy
- Medical history which deemed to affect efficacy.
- Use of prohibited treatment or medication before or during the study which will affect the assessment of efficacy.
- Not receiving randomised treatment.
- Time window deviation
- Treatment Non-compliance

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

Protocol deviations will be listed in Listing 16.2.2.

2.1.3 Analysis populations

Four analysis populations are defined.

Population	Definition / Criteria	Analyses Evaluated
All Screened Subjects	• All subjects those who are screened	• Disposition
Randomised	• All subjects who all are randomised and may or may not receive the application of the study products.	• Protocol deviations
Safety	• Safety population includes all subjects who received any application of the study products.	• Safety analyses
Intent-to-Treat (ITT)	• The 'Intent to treat' ITT population includes all subjects who are randomised into the study and have skin irritation scores from at least one of the test sites available.	• Efficacy analysis

The numbers of subjects included in each of the analysis populations will be presented (Table 14.1.1).

2.1.4 Subgroups/Stratifications

Not Applicable.

2.1.5 Centre pooling

Not Applicable.

2.2 Patient demographics/other baseline characteristics

Demographic and baseline characteristics summaries will be produced for the safety and ITT.

2.2.1 Demographic and Baseline characteristics

Categorical demographic variables include gender, race, ethnicity and Fitzpatrick skin type grading. These variables will be summarized by the number and percentage of subjects with each relevant characteristic in each treatment group (Table 14.1.2.1). Age will be summarised by the mean, standard deviation, median, minimum and maximum values.

The Fitzpatrick scale is a numerical classification that is widely used by dermatologists to classify a person's skin type by their response to the sun exposure (Fitzpatrick, 1988).

2.2.2 General medical history

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

2.2.3 Characteristics of Disease

Not Applicable.

2.3 Treatments (study drug, rescue medication, other concomitant therapies, compliance)

2.3.1 Study Product/drug Compliance and Exposure

Any protocol deviations associated with treatment applications or patch adherence will be listed at the blinded data review stage.

2.3.2 Concomitant medication

Concomitant medication/non-drug treatments data will not be presented in the study report. A data listing will be produced for evaluation of protocol violations only at the blinded data review stage.

2.4 Analysis of Dermal Responses

2.4.1 Primary endpoint

2.4.1.1 Primary endpoint definition

The primary analysis will be conducted to assess the photoirritation and photosensitisation potential of the test and control product, based on the irritation (dermal response) and superficial irritation (other effects) score/grade after patch removal during the induction and challenge phase using the ITT population.

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

The combined score for dermal response and superficial irritation (other effects) 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 2 below, and the superficial irritation scores in Table 3 below.

CCI

[redacted]

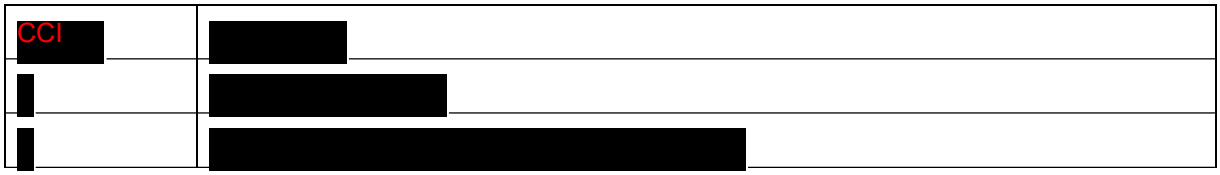
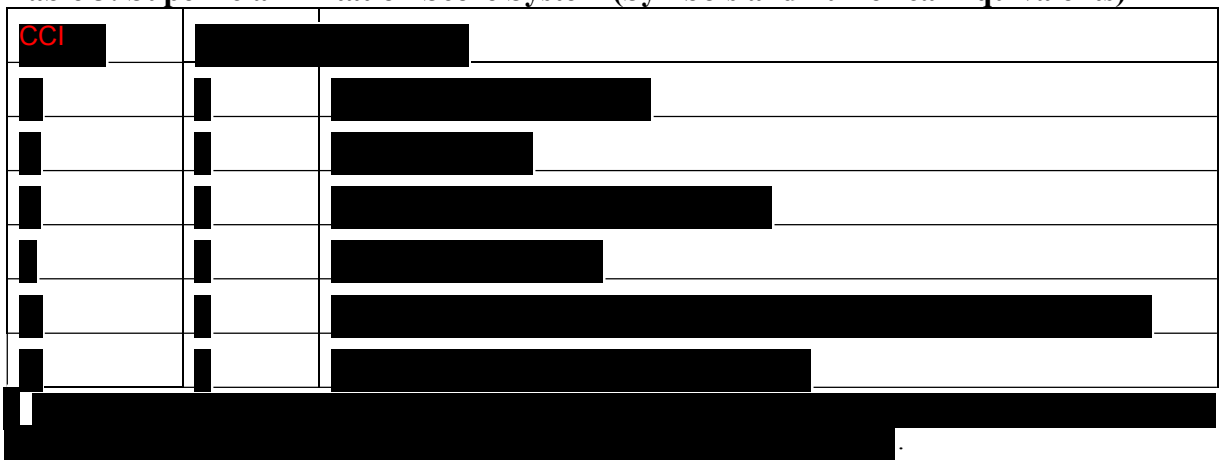


Table 3: Superficial Irritation Score System (Symbols and numerical Equivalents)



Only subjects with at least one combined score > 0 at any visit will be summarised. The frequency of scores will be summarized in each category of combined score by treatment group and at each time point for both induction and challenge phases. The maximum combined score irrespective of visits for each phase will also be presented (Table 14.2.1.1).
No formal statistical inference will be performed.

The frequency of scores will be summarized in each category of score/grade for dermal responses (Table 14.2.2.1) and superficial irritations (Table 14.2.2.2) by treatment group and at each time point for both induction and challenge phases. The maximum score irrespective of visits for each phase will also be presented.

2.4.1.2 Statistical hypothesis, model, and method of analysis

Not Applicable.

2.4.1.3 Supportive analyses

Not Applicable.

2.4.2 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.

2.5 Analysis of secondary objectives

2.5.1 Dermal Response (secondary)

Not Applicable.

2.5.2 Safety

2.5.2.1 Adverse events and Serious Adverse Events

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

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 medication and those causing study discontinuation will be presented in a similar manner (Table 14.3.1.3). For treatment-related AEs, these will also be presented by severity, if applicable (Table 14.3.1.4).

Additionally, all treatment-emergent adverse events will be listed.

Non-fatal serious adverse events and adverse events causing study treatment discontinuation will be listed (Listing 14.3.2.2).

All AEs will be listed in the Listing 16.2.7.1 using randomised population and Listing 16.2.7.2 using Non-randomised subjects.

2.6 Analysis of other variables

Not applicable.

2.7 Interim analysis

No interim analysis is planned.

2.8 Sample size calculation

Approximately 40 healthy subjects will be screened to randomise at least 30 subjects to ensure at least 25 evaluable subjects complete the entire study. This sample size is standard in clinical testing practices and is consistent with the ANVISA guidelines (ANVISA, 2012).

Healthy male and female subjects aged 18 to 65 with no dermatological disorders and with a Fitzpatrick skin phototype II to IV will be enrolled into this study.

3 Changes to the Protocol Defined Statistical Analysis Plan

There were no changes or deviations to the originally planned statistical analysis specified in the protocol version 2.0 [(Dated: 24/Mar/2017)].

4 Appendix 1:

4.1 List of Tables, Listings and Figures

4.2 Tables

Table Number	Table Title (Population)	Template
14.1.1	Subject Disposition by Treatment Group (All Screened Subjects)	Appendix 2
14.1.2.1	Subject Demographics and Baseline Characteristics (Safety Population)	Appendix 2
14.1.2.2	Subject Demographics and Baseline Characteristics (Intent To Treatment Population)	14.1.2.1
14.2.1.1	Frequency of Combined Score by Phase, Visit and Treatment and Maximum Combined Score (Intent To Treatment Population)	Appendix 2
14.2.2.1	Frequency of Dermal Response Score by Phase, Visit and Treatment and Maximum Dermal Response Score (Intent To Treatment Population)	Appendix 2
14.2.2.2	Frequency of Superficial Irritation (other effects) Score by Phase, Visit and Treatment and Maximum Superficial Irritation (other effects) Score (Intent To Treatment Population)	Appendix 2
14.3.1.1	Summary of Treatment emergent Adverse Event by Skin/ Non-Skin System organ Class (SOC) and Preferred Term (PT) (Safety Population)	Appendix 2
14.3.1.2	Treatment emergent Adverse Event by Severity (Safety Population)	Appendix 2
14.3.1.3	Summary of Treatment emergent Treatment Related Adverse Event by Skin/ Non-Skin SOC and PT (Safety Population)	14.3.1.1
14.3.1.4	Treatment emergent Treatment Related Adverse Event by Severity (Safety Population)	14.3.1.2

4.3 Listings

Listing Number	Listing Title (Population)	Template
14.3.2.2	Listing of Serious Adverse Events leading to Discontinuation (Randomised population)	16.2.7.1
16.1.7	Randomization information (Randomised Population)	Appendix 2

Listing Number	Listing Title (Population)	Template
16.2.2	Individual Subjects Protocol Deviations (Randomised Population)	Appendix 2
16.2.7.1	Listing of All Adverse Events (Randomised Population)	Appendix 2
16.2.7.2	Listing of All Adverse Events (Non Randomised Subjects)	16.2.7.1

Note: If there are no data to display generate a null listing.

4.4 Top line Outputs:

Table/Listing Number	Table/Listing/Figure Title (Population)
14.1.1	Subject Disposition by Treatment Group (All Screened Subjects)
14.1.2.1	Subject Demographics and Baseline Characteristics (Safety Population)
14.2.1.1	Frequency of Combined Score by Phase, Visit and Treatment and Maximum Combined Score (Intent To Treatment Population)
14.3.1.1	Summary of Treatment emergent Adverse Event by Skin/ Non-Skin System organ Class (SOC) and Preferred Term (PT) (Safety Population)
14.3.1.3	Summary of Treatment emergent Treatment Related Adverse Event by Skin/ Non-Skin SOC and PT (Safety Population)
16.2.7.1	Listing of All Adverse Events (Randomised Population)

5 Appendix 2:

5.1 Templates for the Tables, Listings and Figures

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:

- Facial micellar cleanser
- Saline Solution

PROTOCOL: 2075857 PROGRAM RUN DATE: DDMONYYYY

TABLE 14.1.1
SUBJECT DISPOSITION BY TREATMENT GROUP

STUDY POPULATION: ALL SCREENED SUBJECTS (N=XX)

	FACIAL MICELLAR CLEANSER N (%)	SALINE SOLUTION N (%)	OVERALL N (%)
TOTAL NUMBER OF SUBJECTS SCREENED			XX (XX.X)
SUBJECTS NOT RANDOMISED			XX (XX.X)
DID NOT MEET STUDY CRITERIA			XX (XX.X)
ADVERSE EVENTS			XX (XX.X)
ETC.			XX (XX.X)
SUBJECTS RANDOMISED	XX (XX.X)	XX (XX.X)	XX (XX.X)
COMPLETED	XX (XX.X)	XX (XX.X)	XX (XX.X)
DID NOT COMPLETE	XX (XX.X)	XX (XX.X)	XX (XX.X)
ADVERSE EVENT	XX (XX.X)	XX (XX.X)	XX (XX.X)
LOST TO FOLLOW UP	XX (XX.X)	XX (XX.X)	XX (XX.X)
PROTOCOL DEVIATIONS	XX (XX.X)	XX (XX.X)	XX (XX.X)
WITHDRAWAL OF CONSENT	XX (XX.X)	XX (XX.X)	XX (XX.X)
OTHER	XX (XX.X)	XX (XX.X)	XX (XX.X)
RANDOMISED POPULATION	XX (XX.X)	XX (XX.X)	XX (XX.X)
SAFETY POPULATION	XX (XX.X)	XX (XX.X)	XX (XX.X)
INTENT TO TREAT POPULATION	XX (XX.X)	XX (XX.X)	XX (XX.X)

PROTOCOL: 207587 PROGRAM RUN DATE: DDMONYYYY

TABLE 14.1.2.1

SUBJECT DEMOGRAPHICS AND BASELINE CHARACTERISTICS

STUDY POPULATION: SAFETY POPULATION (N=XX)

DEMOGRAPHIC VARIABLES	FACIAL MICELLAR CLEANSER (N=XX)	SALINE SOLUTION (N=XX)	OVERALL (N=XX)
SEX N (%)			
MALE	XX (XX.X)	XX (XX.X)	XX (XX.X)
FEMALE	XX (XX.X)	XX (XX.X)	XX (XX.X)
RACE N (%)			
AMERICAN INDIAN OR ALASKA NATIVE	XX (XX.X)	XX (XX.X)	XX (XX.X)
AFRICAN AMERICAN/AFRICAN HERITAGE	XX (XX.X)	XX (XX.X)	XX (XX.X)
ASIAN - CENTRAL/SOUTH ASIAN HERITAGE	XX (XX.X)	XX (XX.X)	XX (XX.X)
ASIAN - EAST ASIAN HERITAGE	XX (XX.X)	XX (XX.X)	XX (XX.X)
ASIAN - JAPANESE 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
FITZPATRICK SCALE FOR SKIN TYPE			
ALWAYS BURNS EASILY; NEVER TANS (PALE WHITE SKIN)	XX (XX.X)	XX (XX.X)	XX (XX.X)
ALWAYS BURNS EASILY; TANS MINIMALLY (WHITE SKIN)	XX (XX.X)	XX (XX.X)	XX (XX.X)
BURNS MODERATELY; TANS GRADUALLY (LIGHT BROWN SKIN)	XX (XX.X)	XX (XX.X)	XX (XX.X)
BURNS MINIMALLY, ALWAYS TANS WELL (MODERATE BROWN SKIN)	XX (XX.X)	XX (XX.X)	XX (XX.X)
RARELY BURNS, TANS PROFUSELY (DARK BROWN SKIN)	XX (XX.X)	XX (XX.X)	XX (XX.X)
NEVER BURNS (DEEPLY PIGMENTED DARK BROWN TO BLACK SKIN)	XX (XX.X)	XX (XX.X)	XX (XX.X)

PROTOCOL: 207587 PROGRAM RUN DATE: DDMONYYYY

TABLE 14.2.1.1
FREQUENCY OF COMBINED SCORE BY PHASE, VISIT AND TREATMENT AND MAXIMUM COMBINED SCORE

STUDY POPULATION: INTENT TO TREAT POPULATION (N=XX)
PHASE: INDUCTION PHASE

VISIT	COMBINED SCORES	FACIAL MICELLAR CLEANSER (N=XX) N	SALINE SOLUTION (N=XX) N
SUBJECTS WITH AT LEAST ONE COMBINED SCORE > 0 AT ANY VISIT N (%)		XX (XX.X)	XX (XX.X)
SUBJECTS WITH NO COMBINED SCORE > 0 AT ANY VISIT N (%)		XX (XX.X)	XX (XX.X)
VISIT 2	0	XX	XX
	1	XX	XX
	2	XX	XX
	3	XX	XX
	4	XX	XX
	5	XX	XX
	6	XX	XX
	7	XX	XX
VISIT 3		XX	XX
		XX	XX
		XX	XX
VISIT 13		XX	XX
		XX	XX
MAXIMUM COMBINED SCORE	1	XX	XX
	2	XX	XX
	3	XX	XX
	4	XX	XX
	5	XX	XX
	6	XX	XX
	7	XX	XX

COMBINED SCORE: DERMAL RESPONSE SCORE + SUPERFICIAL RESPONSE SCORE (>0)

PPD PPD

Programming Note:

- Induction Phase include Visit 2 (Visit 1 and Visit 2 could be combined) till Visit 13.

- Rest Phase include Visit 14
- Challenge Phase include Visit 15 till Visit 19.
- This table is only required if at least one subject reports a combined score >0
- Maximum combined Score will be calculated and displayed at the end of each phase irrespective of visits.

PROTOCOL: 207587 PROGRAM RUN DATE: DDMONYYYY

TABLE 14.2.2.1
FREQUENCY OF DERMAL RESPONSE SCORE BY PHASE, VISIT AND TREATMENT AND MAXIMUM DERMAL RESPONSE SCORE

STUDY POPULATION: INTENT TO TREAT POPULATION (N=XX)
PHASE: INDUCTION PHASE

VISIT		FACIAL MICELLAR CLEANSER (N=XX) N	SALINE SOLUTION (N=XX) N
SUBJECTS WITH AT LEAST ONE DERMAL RESPONSE SCORE > 0 AT ANY VISIT N (%)		XX (XX.X)	XX (XX.X)
SUBJECTS WITH NO DERMAL RESPONSE SCORE > 0 AT ANY VISIT N (%)		XX (XX.X)	XX (XX.X)
VISIT 2	SCORE=0	XX	XX
	SCORE=1	XX	XX
	SCORE=2	XX	XX
	SCORE=3	XX	XX
	SCORE=4	XX	XX
	SCORE=5	XX	XX
	SCORE=6	XX	XX
	SCORE=7	XX	XX
VISIT 3	….		
VISIT 4	…		
……..			
VISIT 13	…		
……			
MAXIMUM DERMAL RESPONSE SCORE	….		

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

PPD

Programming Note:

- Induction Phase include Visit 2 (Visit 1 and Visit 2 could be combined) till Visit 13.
- Repeat table for Challenge phase. Challenge Phase include Visit 15 till Visit 19
- This table is only required if at least one subject reports a dermal response score >0
- Maximum dermal response Score will be calculated and displayed at the end of each phase irrespective of visit

PROTOCOL: 207587 PROGRAM RUN DATE: DDMONYYYY

TABLE 14.2.2.2
FREQUENCY OF SUPERFICIAL IRRITATION (OTHER EFFECTS) SCORE BY PHASE, VISIT AND TREATMENT AND MAXIMUM SUPERFICIAL IRRITATION (OTHER EFFECTS) SCORE

STUDY POPULATION: INTENT TO TREAT POPULATION (N=XX)
PHASE: INDUCTION PHASE

VISIT		FACIAL MICELLAR CLEANSER (N=XX) N	SALINE SOLUTION (N=XX) N
SUBJECTS WITH AT LEAST ONE SUPERFICIAL IRRITATION SCORE > 0 AT ANY VISIT N (%)		XX (XX.X)	XX (XX.X)
SUBJECTS WITH NO SUPERFICIAL IRRITATION SCORE > 0 AT ANY VISIT N (%)		XX (XX.X)	XX (XX.X)
VISIT 2	GRADE=A/SCORE=0	XX	XX
	GRADE=B/SCORE=1	XX	XX
	GRADE=C/SCORE=2	XX	XX
	GRADE=F/SCORE=3	XX	XX
	GRADE=G/SCORE=3	XX	XX
	GRADE=H/SCORE=3	XX	XX
VISIT 3	SAME AS ABOVE		
VISIT 4	SAME AS ABOVE		
……..			
VISIT 13	SAME AS ABOVE		
……..			
MAXIMUM SUPERFICIAL IRRITATIONSCORE	SAME AS ABOVE	XX	XX

A/0 = SLIGHT GLAZED APPEARANCE; B/1 = MARKED GLAZING; C/2 = GLAZING WITH PEELING AND CRACKING F/3 = GLAZING WITH FISSURES' G/3 = FILM OF DRIED SEROUS EXUDATE COVERING ALL OR PORTION OF THE PATCH; H/3 = SMALL PETECHIAL EROSIONS AND/OR SCABS

PPD

Programming Note:

- Induction Phase include Visit 2 (Visit 1 and Visit 2 could be combined) till Visit 13.
- Repeat table for challenge phase. Challenge Phase include Visit 15 till Visit 159
- This table is only required if at least one subject reports a superficial irritation score >0
- Maximum superficial irritation Score will be calculated and displayed at the end of each phase irrespective of visits.

PROTOCOL: 207587 PROGRAM RUN DATE:DDMONYYYY

TABLE 14.3.1.1
SUMMARY OF TREATMENT EMERGENT ADVERSE EVENT BY SKIN/ NON-SKIN SYSTEM ORGAN CLASS (SOC) AND PREFERRED TERM (PT)

STUDY POPULATION: SAFETY POPULATION (N=XX)

SYSTEM ORGAN CLASS PREFERRED TERM	FACIAL MICELLAR CLEANSER (N=XX)		SALINE SOLUTION (N=XX)		OVERALL (N=XX)	
	N (%)	NAE	N (%)	NAE	N (%)	NAE
NUMBER OF SUBJECTS WITH AT LEAST ONE AE	XX (XX.X)	XX	XX (XX.X)	XX	XX (XX.X)	XX
NUMBER OF SUBJECTS WITH NO AE	XX (XX.X)	XX	XX (XX.X)	XX	XX (XX.X)	XX
SKIN RELATED AES	XX (XX.X)	XX	XX (XX.X)	XX	XX (XX.X)	XX
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	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
DERMATITIS	XX (XX.X)	XX	XX (XX.X)	XX	XX (XX.X)	XX
NON SKIN RELATED AES	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
ABDOMINAL PAIN	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
VOMITTING	XX (XX.X)	XX	XX (XX.X)	XX	XX (XX.X)	XX

N (%) = NUMBER (PERCENT) OF SUBJECTS NAE = NUMBER OF ADVERSE EVENTS.

PROTOCOL: 2075857 PROGRAM RUN DATE: DDMONYYYY

TABLE 14.3.1.2
SUMMARY OF TREATMENT EMERGENT ADVERSE EVENT BY SEVERITY

STUDY POPULATION: SAFETY POPULATION (N=XX)

SYSTEM ORGAN CLASS / PREFERRED TERM	FACIAL MICELLAR CLEANSER (N=XX)						SALINE SOLUTION (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 AE	XX (XX.X)	XX	XX (XX.X)	XX	XX (XX.X)	XX	XX (XX.X)	XX	XX (XX.X)	XX	XX (XX.X)	XX
NUMBER OF SUBJECTS WITH NO AE	XX (XX.X)	XX	XX (XX.X)	XX	XX (XX.X)	XX	XX (XX.X)	XX	XX (XX.X)	XX	XX (XX.X)	XX
SKIN RELATED AES	XX (XX.X)	XX	XX (XX.X)	XX	XX (XX.X)	XX	XX (XX.X)	XX	XX (XX.X)	XX	XX (XX.X)	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
NON SKIN RELATED AES	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.

PPD PPD

PROTOCOL: 2075857 PROGRAM RUN DATE: DDMONYYYY

LISTING 16.1.7
RANDOMIZATION INFORMATION

STUDY POPULATION: RANDOMISED POPULATION (N=XX)

SUBJECT NUMBER	TREATNMENT SEQUENCE [1]	RANDOMIZATION NUMBER	RANDOMIZATION DATE
PPD	PPD		DDMMYYYY

[1] A= FACIAL MICELLAR CLEANSER; B= SALINE SOLUTION

PROTOCOL: 207587 PROGRAM RUN DATE: DDMONYYYY

LISTING 16.2.1
INDIVIDUAL SUBJECTS PROTOCOL DEVIATIONS

STUDY POPULATION: RANDOMISED POPULATION (N=XX)

TREATMENT GROUP: SALINE SOLUTION

SUBJECT NUMBER	AGE/SEX/RACE[1]	VISIT #	DEVIATION SEQUENCE	PROTOCOL VIOLATION
PPD		VISIT 3	1	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.

PPD PPD

PROTOCOL: 207587 PROGRAM RUN DATE: DDMONYYYY

LISTING 16.2.7.1
LISTING OF ALL ADVERSE EVENT

STUDY POPULATION: RANDOMISED POPULATION (N=XX)
TREATMENT GROUP: FACIAL MICELLAR CLEANSER

SUBJECT NUMBER	AGE/SEX/RACE[1]	SITE	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 ?	OUTCOME	ACTION TAKEN RE STUDY PRODUCT	SERIOUS?	WITHDREW ? [4]
PPD	PPD		ERYTHEMA	31MAR2017 /3	9:00	31MAR 2017	11:00	MILD	NO	RESOLVED		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, 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?

PPD PPD

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.