**CONFIDENTIAL**

# STATISTICAL ANALYSIS PLAN FOR PROTOCOL 207585

A Human Repeat Insult Patch Test (HRIPT) in Healthy Subjects to Assess the Cutaneous Irritation and Sensitisation Potential of a Cosmetic Facial Product

**BIOSTATISTICS DEPARTMENT**

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Document type: Statistical Analysis Plan


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Document status: Final 1.0

Release date: 09-May-2017

The purpose of this Statistical Analysis Plan is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 207585. The SAP will be finalized prior to data base freeze and treatment code un-blinding.

# 1 Study details

The purpose of this trial is to assess the cutaneous irritation and sensitisation potential of a cosmetic facial product by following a conventional Human Repeated Insult Patch Test (HRIPT) methodology under supervision of a dermatologist.

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

This is a single-center, randomised, assessor blind study in healthy subjects aged 18-65 years, with a Fitzpatrick skin type phototype of I to IV. Subjects will be exposed to repeated insult dermal semi-occlusive patch applications of a cosmetic facial skin product and negative control (saline solution).

## 1.1 Study design

| **Overall Design** |
|---|
| Test site randomised, assessor-blinded, single-center, HRIPT in healthy subjects to assess the cutaneous irritation and sensitisation potential of a cosmetic facial product, by following a conventional HRIPT methodology under supervision of a dermatologist. |
| **Day -14 to 0 / Visit 1 - Screening Visit**<br>**NOTE: Visit 1 and Visit 2 could be combined** |
| The following assessments will be conducted:<br>1. Subject Informed Consent taken<br>2. Subject demographics collected<br>3. Medical history details<br>4. Details of current and concomitant medication collected<br>5. Fitzpatrick Skin Type Assessment (Appendix 3 of the protocol)<br>6. Inclusion/Exclusion criteria<br>7. Dermatologist determination for eligibility to participate in the study (including visual examination of the dorsum scapular region)<br>8. Subject Eligibility |
| **Day 1 to 22/ Visit 2 – Visit 11 – Induction Phase (3 Weeks)**<br>**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 (3c only at Visit 2 if Visit 1 and 2 are no 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 (Visit 2/Day 1 only) as per Appendix 2 of the Protocol.
7. Patch applications (9 patch applications to the same test site, over 3 consecutive weeks with patches applied on alternate weekdays).
8. Patch removal after 48 (± 2) hours or 72 (± 2) hours over inclusive weekends.
9. Reaction grading/assessment performed by a qualified staff member, as per Appendix 2 of the Protocol.
10. Adverse event assessment

**Note:** 30 minutes (maximum of 1 hour) after patch removal, sites will be graded/evaluated, then patches will be reapplied to the same sites.

**Day 22 – Day 36/ Visit 11 – Visit 12 – Rest Phase (2 Weeks)**

**No Patch Application**

**Days 36 to 39 / Visit 12 to Visit 14 - 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 12/Day 36).
4. Challenge Phase patch application to naïve site (Visit 12/Day 36).
5. Patch removal 48 (± 2) or 72 (± 2) hours over inclusive weekends after application. (Visit 13/Day 38).
6. Reaction grading/assessment performed by a qualified staff member at approximately 30 minutes (maximum 1 hour) after patch removal.
7. 24 (± 2) hours after patch removal (Visit 14/Day 39) subjects will return for assessment performed by a qualified staff member.
8. Adverse event assessment.

**Day 40 / Visit 15 – End of Study**

The following assessments will be conducted:

1. Current/Concomitant Medications review
2. Adverse event assessment.
3. 48 (± 2) hours after patch removal (Visit 15/Day 40) final challenge patch site assessment performed by a qualified staff member.
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 irritation and contact sensitisation 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 | N/A<br>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 a total of 9 patch applications, over 3 consecutive weeks, with patches applied on alternate weekdays each week (Monday, Wednesday, and Friday). Each patch will contain the test product and saline solution. Each patch will remain in place for 48 (± 2) hours on weekdays and 72 hours on weekends. The patch will be removed and the area will be cleaned with saline solution. After 30 minutes (maximum of 1 hour) the site will be graded/evaluated as per the scale in Appendix 2. A new patch of both test product and saline solution will then be reapplied to the same site.

There will then be a two week rest period where no patch applications or assessments are made.

During the Challenge Phase, a naïve site (previously un-patched area) will be selected for the Challenge patch, this area will be graded/evaluated prior to any patch application. A patch with the test product and saline solution will then be randomly applied to the selected previously untreated areas of skin according to the subject's random assignment as determined on Day 1 of the Induction phase. After 48 (± 2) hours, each subject will return for Challenge patch removal, the site will be cleaned with saline solution and graded/evaluated after 30 minutes (maximum of 1 hour). Subjects will return after 24 (± 2) hours and 48 (± 2) hours post patch removal for further grading/assessment.

## 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 will remain in place | 48 (± 2) hours during the week |
| | Patches applied on Friday will remain in place | 72 (± 2) hours until Monday |
| | Assessment after patch removal | 30 minutes (up to 1 hour) |
| Challenge phase | Patches will remain in place | 48 (± 2) hours during the week |
| | Assessment after patch removal | 30 minutes (up to 1 hour) |
| | Further assessment after patch removal | 24(±2), 48 (± 2) hours |

# 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.

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

## 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 violations

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

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

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.

### 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 violations |
| Safety | • Safety population includes all subjects who are randomized and 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 |

### 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 and Fitzpatrick score. These variables will be summarized by the number and percentage of subjects with each relevant characteristic (Table 14.1.2). Age will be summarized 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).

**Table 1: Fitzpatrick Scale For The Assessment Of Skin Type**

CII


### 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)

Not Applicable.

### 2.3.1 Study Product/drug Compliance and Exposure

Any protocol deviation 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 cutaneous irritation and sensitisation potential of the test and control product, based on the combined irritation (dermal response) and superficial irritation (other effects) score/grade after patch removal during the induction and challenge phases 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.

**Table 2: Skin Irritation Scoring System (Dermal Response)**

CII

[redacted]

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

CII

[redacted]

* The letter grades assigned to the irritation responses will be converted to scores for the statistical analysis process. Grading will be conducted throughout the trial by a qualified staff member.

For example, if the dermal responses score=3 and superficial irritation letter =”C” then the combined score will be:

Combined score = 3 + 2 = 5

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.

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 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 and Listing 16.2.7.2

## 2.6 Analysis of other variables

Not applicable.

## 2.7 Interim analysis

No interim analysis is planned.

## 2.8 Sample size calculation

Approximately 280 healthy subjects were screened to randomize at least 240 subjects to ensure 200 evaluable subjects complete the entire study. If no reaction is observed in 200 subjects, there is a 95% certainty that the actual rate of reactions in the wider population is <1.8%.

# 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 1.0 [(Dated: 31/JAN/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 (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 (ITT Population) | 14.1.2.1 |
| 14.2.1.1 | Frequency of Combined Score by Phase, Visit and Treatment and Maximum Combined Score (ITT Population) | Appendix 2 |
| 14.2.2.1 | Frequency of Dermal Response Score by Phase, Visit and Treatment and Maximum Dermal Response Score (ITT 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 (ITT Population) | Appendix 2 |
| 14.3.1.1 | Treatment emergent Adverse Event (Safety Population) | Appendix 2 |
| 14.3.1.2 | Treatment emergent Adverse Event by Severity (Safety Population) | Appendix 2 |
| 14.3.1.3 | Treatment emergent Treatment Related Adverse Event (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 |
|---|---|---|
| 14.3.2.1 | Listing of Deaths (Randomised Population) | 16.2.7.1 |
| 14.3.2.2 | Listing of Serious Adverse Events leading to Discontinuation (Randomised Population) | 16.2.7.1 |
| 16.1.7 | Randomisation information (Randomised Population) | Appendix 2 |
| 16.2.2 | Individual Subjects Protocol Violation (Randomised Population) | Appendix 2 |

| Listing Number | Listing Title (Population) | Template |
|---|---|---|
| 16.2.7.1 | All Adverse Events (Randomised Population) | Appendix 2 |
| 16.2.7.2 | 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 Figure Number | Table/Listing/Figure Title (Population) |
|---|---|
| 14.1.1 | Subject Disposition (All Screened Subjects) |
| 14.1.2 | Subject Demographics (ITT Population) |
| 14.2.1.1 | Frequency of Combined Score by Phase, Visit and Treatment and Maximum Combined Score (ITT Population) |
| 14.3.1.1 | Treatment emergent Adverse Event (Safety Population) |
| 16.2.7.1 | 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

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Table 14.1.1
Subject Disposition
All Screened Subjects

All Screened Subjects (N=XX)

| | Overall(N=XX) 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) |
| COMPLETED | xx (xx.x) |
| DID NOT COMPLETE | xx (xx.x) |
| ADVERSE EVENT | xx (xx.x) |
| LOST TO FOLLOW UP | xx (xx.x) |
| PROTOCOL DEVIATION | xx (xx.x) |
| WITHDRAWAL OF CONSENT | xx (xx.x) |
| OTHER | xx (xx.x) |
| RANDOMISED POPULATION | xx (xx.x) |
| SAFETY POPULATION | xx (xx.x) |
| INTENT TO TREAT POPULATION | xx (xx.x) |

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Table 14.1.2.1
Subject Demographics and Baseline Characteristics
Safety Population

Safety Population (N=XX)

| Demographic variables | Overall (N=XX) |
|---|---|
| SEX n (%) | |
| MALE | xx (xx.x) |
| FEMALE | xx (xx.x) |
| RACE n (%) | |
| ASIAN | xx (xx.x) |
| BLACK or AFRICAN | xx (xx.x) |
| AMERICAN INDIAN OR ALASKA NATIVE | xx (xx.x) |
| NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER | xx (xx.x) |
| WHITE | xx (xx.x) |
| MULTIPLE | xx (xx.x) |
| AGE (YEARS) | |
| N | XX |
| MEAN | XX.X |
| SD | XX.XX |
| MEDIAN | XX.X |
| MINIMUM | XX |
| MAXIMUM | XX |
| FITZPATRICK SCALE FOR SKIN TYPE | |
| I= ALWAYS BURNS EASILY NEVER TANS (PALE WHITE SKIN); | xx (xx.x) |
| II= ALWAYS BURNS EASILY; TANS MINIMALLY (WHITE SKIN); | xx (xx.x) |
| III= BURNS MODERATELY; TANS GRADUALLY (LIGHT BROWN SKIN); | xx (xx.x) |
| IV= BURNS MINIMALLY, ALWAYS TANS WELL (MODERATE BROWN SKIN); | xx (xx.x) |
| V= RARELY BURNS, TANS PROFUSELY (DARK BROWN SKIN); | xx (xx.x) |
| VI= NEVER BURNS (DEEPLY PIGMENTED DARK BROWN TO BLACK SKIN) | xx (xx.x) |

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Table 14.2.1.1
Frequency of Combined Score by Phase, Visit and Treatment and Maximum Combined Score
Intent to Treat 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 10 | | 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)

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**Programming Note:**

- Induction Phase include Visit 2 till Visit 10.
- Rest Phase include Visit 11
- Challenge Phase include Visit 12 till Visit 15
- 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.

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Table 14.2.2.1
Frequency of Dermal Response Score by Phase, Visit and Treatment and Maximum Dermal Response Score
Intent to Treat Population

Intent to Treat Population (N=XX)

Phase: Induction Phase

| Visit | Score | 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 | | | |
| | 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 | | | |
| VISIT 4 | | | |
| …….. | | | |
| VISIT 10 | | | |
| MAXIMUM DERMAL RESPONSE SCORE | | 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



PPD

**Programming Note:**

- Induction Phase include Visit 2 till Visit 10.
- Rest Phase include Visit 11
- Repeat for the challenge phase.
- Challenge Phase include Visit 12 till Visit 15
- 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 visits.

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Table 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 Treat Population

Intent to Treat Population (N=XX)

Phase: Induction Phase

| Visit | Grade/Score | 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 | ..... | | |
| VISIT 4 | ..... | | |
| …….. | | | |
| VISIT 10 | ..... | | |
| MAXIMUM SUPERFICIAL IRRITATION SCORE | ..... | 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

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PPD

**Programming Note:**

- Induction Phase include Visit 2 till Visit 10.
- Rest Phase include Visit 11
- Repeat for the challenge phase.
- Challenge Phase include Visit 12 till Visit 15
- 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.

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Table 14.3.1.1
Summary of Treatment emergent Adverse Event
Safety Population

Safety Population (N=xx)

| System Organ Class<br>Preferred Term | Facial micellar cleanser (N=XX) | | Saline Solution (N=XX) | |
|---|---|---|---|---|
| | n (%) | nAE | n (%) | nAE |
| NUMBER OF SUBJECTS WITH AT LEAST ONE AE | xx (xx.x) | xx | xx (xx.x) | xx |
| NUMBER OF SUBJECTS WITH NO AE | xx (xx.x) | xx | xx (xx.x) | xx |
| SKIN RELATED AES | 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 |
| NON SKIN RELATED AES | 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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Table 14.3.1.2
Summary of Treatment emergent Adverse Event by Severity
Safety Population

Safety Population (N=xx)

| System Organ Class<br>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.

Protocol: 207585 Program Run Date:ddmonyyyy

Listing 16.1.7
Randomisation information
Randomised Population

| Subject Number | Age/Sex/Race[1] | Randomisation Number | Test Site/Treatment Randomised | Date of randomization |
|---|---|---|---|---|
| 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.

Page x of y

PPD

Protocol: 207585 Program Run Date:ddmonyyyy

Listing 16.2.2
Individual Subjects Protocol Violation
Randomised Population

| Subject Number | Age/Sex/Race[1] | Phase/Visit #[2] | Violation Sequence | Protocol Violation |
|---|---|---|---|---|
| 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] Induction phase: Visit 2 till Visit 10; Rest: Visit 11; Challenge phase: Visit 12 till Visit 15.

Protocol: 207585 Program Run Date:ddmonyyyy

Listing 16.2.7.1
All Adverse Events
Randomised Population

Treatment Group: Facial micellar cleanser

| 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?



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.