CONFIDENTIAL

STATISTICAL ANALYSIS PLAN FOR PROTOCOL 207235

A Human Subject 24 Hour Patch Test to Assess the
Irritation Potential of Four Skin Serum Products

BIOSTATISTICS DEPARTMENT
GLAXOSMITHKLINE CONSUMER HEALTHCARE

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The purpose of this Statistical Analysis Plan (SAP) is to describe the planned analyses and output to be included in the Clinical Study Report for Clinical Study Protocol (CSP) 207235. This SAP will be finalized prior to database 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. For this reason, the raw materials used in a product formulation must be raw materials with proven safety and tolerability. As a general requirement the safety and tolerability of a final formulation must be confirmed before it is marketed. (Guideline for the Safety Evaluation of Cosmetic Products; Agência Nacional de Vigilância Sanitária (ANVISA) 2012).

Skin contact with topical products such as cosmetics may trigger different types of reactions including eczematous, contact dermatitis, urticaria, acne and spots. Contact dermatitis can arise from two mechanisms: primary irritation, through the action of irritant substances; or sensitization, in the presence of an allergenic ingredient (Birmingham, 1965).

Tests to evaluate the irritation and sensitization potential of a product must take into account a number of variables including the components used in the formulation concentration, absorption, amount applied, skin condition, application directions and frequency, as well as any cumulative effects (Dooms-Goossens, 1993).

Primary irritation results from a direct chemical attack on the skin and is characteristically a rapid response, occurring on first contact with the skin. The effect may be limited to the stratum corneum and may result in symptoms such as dryness,flaking, or cracking. Primary irritation may involve deeper penetration, through the epidermis and into the dermis, where the classic inflammatory response takes place with erythema (reddening) and possibly edema (swelling), vesiculation (blistering) or exudation (weeping).

The human patch test is a well-established industry test for assessing primary skin irritation potential. The products are applied via an occlusive or semi-occlusive patch.

This occlusion provides a higher contact between the components of the product formula and the skin.

This clinical study is being performed to assess the primary irritation potential of the four study products. A standard saline solution will also be included as a negative control.

The study will be considered a success if no irritation is observed which is attributable to the test product at any time point, or if any observed irritation for the test product is not clinically differentiable from the saline solution.

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

1.1 Study design

This is an evaluator (single) blind, single site, randomized and intra-subject comparison patch test study to evaluate the cutaneous irritation potential of four experimental daily defense serum formulations, including a saline solution as a negative control.

Subjects will be exposed to 24 hour semi-occlusive patch applications of the test products and negative control. At all study visits, subjects will be asked by a trained technician if there have been any feelings of discomfort since the last visit, and also if any medication has been taken during this period.

1.2 Study objectives

Objectives	Endpoints
Primary Objective	**Primary Endpoint**
To assess the irritation potential of four prototype daily defense serum formulations after 24 (± 2) hours under semi-occlusive patch application to the skin of healthy volunteers.	Trained evaluator assessment of product tolerability through visual assessment of cutaneous irritation 15-30 minutes, 24 +/- 2 and 48 +/-2 hours after patch removal.
Secondary Objectives	**Secondary Endpoints**
To evaluate the general safety of four prototype daily defense serum formulations.	Frequency and severity of Adverse Events.

1.3 Treatments

	Test product 1	**Test product 2**	**Test product 3**	**Test Product 4**	**Reference product**
Product Name	Experimental Daily Defense Serum A	Experimental Daily Defense Serum C	Experimental Daily Defense Serum G	Experimental Daily Defense Serum N	Saline Solution Sodium Chloride ($NaCl_{aq}$; 0.9%)
Product Formulation Code (MFC)	CCI [redacted]	CCI [redacted]	CCI [redacted]	CCI [redacted]	N/A

	Test product 1	Test product 2	Test product 3	Test Product 4	Reference product
Dose	$0.02ml/cm^2$				
Route of Administration	Topical application via semi occlusive patch				

1.4 Timepoints and visit windows

Deviations from the scheduled assessment times should be avoided or kept to a minimum as possible. The following are the assessment time windows.

Visit	Activity	Time window
Visit 3 (Day2)	Patch Removal	24 (± 2hrs) after application on Day 1
	Test Site Assessment	15~30 mins after patch removal
Visit 4 (Day3)	Test Site Assessment	24 (± 2hrs) after patch removal on Day 2
Visit 5 (Day4)	Test Site Assessment	48 (± 2hrs) after patch removal on Day 2

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.

Expect 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

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

Major violations will be defined in the "Review Listing Requirement (RLR)" document.

A list of protocol deviations will be provided (Listing 16.2.2).

2.1.3 Analysis populations

Four populations are defined below.

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

2.1.4 Subgroups/Stratifications

Not applicable.

2.1.5 Centers pools

Not applicable.

2.2 Patient demographics/other baseline characteristics

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

2.2.1 Demographic 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 14.1.2.1 for safety, Table 14.1.2.2 for ITT). 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

Skin Type	Sunburn and Tanning History

Skin Type	Sunburn and Tanning History
I	Always burns easily; never tans (pale white skin)
II	Always burns easily; tans minimally (white skin)
III	Burns moderately; tans gradually (light brown skin)
IV	Burns minimally, always tans well (moderate brown skin)
V	Rarely burns, tans profusely (dark brown skin)
VI	Never burns (deeply pigmented dark brown to black skin)

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 skin irritation

2.4.1 Primary endpoint

2.4.1.1 Primary skin irritation endpoint definition

The primary analysis will be based on the irritation scores assessed using the dermal scale described below.

Table 2: Skin Irritation Scoring System − Dermal Response

Score	Skin Appearance
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

Summary statistics will be presented by product group for skin irritation scores at 15-30 mins, 24 and 48 hours after patch removal. Number and percentage of subjects recording each category of skin irritation score will be presented in Table 14.2.1.1. Mean, median, min and max irritation scores will be presented in Table 14.2.1.2.

2.4.1.2 Statistical hypothesis, model, and method of analysis

Not applicable. No formal statistical inference will be performed.

2.4.2 Secondary skin irritation endpoint

2.4.2.1 Secondary skin irritation endpoint definition and analysis

Secondary analysis will include effect on superficial layers of the skin as defined below.

Table 3: Skin Irritation Scoring System – Other Effects

Score (Numeric equivalent)	Observation
A (0)	Slight glazed appearance
B (1)	Marked glazed appearance
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 site
H (3)	Small petechial erosions and/or scabs

A combined dermal response and other effect score will be derived as the sum of Dermal Response Score plus numerical equivalent for the "Other Effect" lettered score. As an example, if dermal response score=3 and superficial irritation letter ="C" then the combined score will be 3 + 2 = 5. This combined score will also be summarized descriptively as the number and percent of subjects reporting/developing each category of score (Table 14.2.2.1).

"Other effect" score will be summarized descriptively as the number and percent of subjects reporting each category of score (Table 14.2.2.2).

2.4.3 Handling of missing values/censoring/discontinuations

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

2.5 Analysis of secondary objectives

Not applicable.

2.6 Safety

2.6.1.1 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), defined as the AEs reported after study product application, 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 emergent-related AEs, these will also be presented by severity, if applicable (Table 14.3.1.4).

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

2.7 Analysis of other variables

Not applicable.

2.8 Interim analysis

No interim analysis is planned.

2.9 Sample size calculation

No statistical analyses will be performed in this study. Approximately 40 subjects will be randomized to ensure at least 30 evaluable subjects complete the study. The number of subjects to be assessed (N=30 completing the study) was based on clinical considerations.

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 3.0 [(Dated: 7/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 (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 Dermal Response Score by Visit and Treatment (ITT Population)	Appendix 2
14.2.1.2	Average Dermal Response Score by Visit and Treatment (ITT Population)	Appendix 2
14.2.2.1	Frequency of Superficial Irritation (other effects) Score by Visit and Treatment (ITT Population)	Appendix 2
14.2.2.2	Frequency of Combined Score by Visit and Treatment (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
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)
14.1.2.2	Subject Demographics (ITT Population)
14.2.1.1	Frequency of Dermal Response Score by Visit and Treatment (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:

- Serum A
- Serum C
- Serum G
- Serum N
- 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)

	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)

	Overall (N=XX)
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 Dermal Response Score by Visit and Treatment
Intent to Treat Population

Intent to Treat Population(N=XX)

Visit	Score	Serum A (N=XX)	Serum C...Serum N (N=XX)...(N=XX)	Saline Solution (N=XX)
VISIT 3 (15~30 min)				
	Missing	xx (xx%)	... ...	xx (xx%)
	0	xx (xx%)	... ...	Xx (xx%)
	1	xx (xx%)	... ...	xx (xx%)
	2	xx (xx%)	... ...	xx (xx%)
	3	xx (xx%)	... ...	xx (xx%)
	4	xx (xx%)	... ...	xx (xx%)
	5	xx (xx%)	... ...	xx (xx%)
	6	xx (xx%)	... ...	xx (xx%)
	7	xx (xx%)	... ...	xx (xx%)
VISIT 4 (24 hours)	Same as above			
VISIT 5 (48 hours)	Same as above			

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

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Table 14.2.1.2
Average Dermal Response Score by Visit and Treatment
Intent to Treat Population

Intent to Treat Population(N=XX)

Visit	variable	Serum A (N=XX)	Serum C...Serum N (N=XX)...(N=XX)	Saline Solution (N=XX)
VISIT 3 (15~30 min)				
	N (non-missing)	xx	... ...	xx
	Mean	x.x	... ...	x.x
	SD	x.xx	... ...	x.xx
	Median	x	... ...	x
	Min	X	... ...	x
	Max	X	... ...	X
VISIT 4 (24 hours)	Same as above			
VISIT 5 (48 hours)	Same as above			

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Note: This table will be provided only if there are subjects with dermal responses > 0.

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Table 14.2.2.1
Summary of Combined Score by Visit and Treatment
Intent to Treat Population

Intent to Treat Population (N=XX)

Visit	Combined Scores	Serum A (N=XX)	Serum C...Serum N (N=XX)...(N=XX)	Saline Solution (N=XX)
VISIT 3 (15~30 min)	0	xx (xx%)	... ...	xx (xx%)
	1	Xx (xx%)	... ...	Xx (xx%)
	2	xx (xx%)	... ...	xx (xx%)
	3	xx (xx%)	... ...	xx (xx%)
	4	xx (xx%)	... ...	xx (xx%)
	5	xx (xx%)	... ...	xx (xx%)
	6	xx (xx%)	... ...	xx (xx%)
	7	xx (xx%)	... ...	xx (xx%)
	...	...	... ...	...
VISIT 4(24 hours)	same as above			
Visit 5 (48 hours)	Same as above			

Combined Score: Dermal response Score + "other effect" score(>0)

PPD

Note: This table will be provided only if there are subjects with combined scores > 0 .

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Table 14.2.2.2
Frequency of Superficial Irritation (other effects score) by Visit and Treatment
Intent to Treat Population

Intent to Treat Population (N=XX)

Visit	Grade/Score	Serum A (N=XX)	Serum C...Serum N (N=XX)...(N=XX)	Saline Solution (N=XX)
VISIT3 (15~30 min)				
	Missing	xx (xx%)	... ...	xx (xx%)
	GRADE=A/SCORE=0	xx (xx%)	... ...	xx (xx%)
	GRADE=B/SCORE=1	xx (xx%)	... ...	xx (xx%)
	GRADE=C/SCORE=2	xx (xx%)	... ...	xx (xx%)
	GRADE=F/SCORE=3	xx (xx%)	... ...	xx (xx%)
	GRADE=G/SCORE=3	xx (xx%)	... ...	xx (xx%)
	GRADE=H/SCORE=3	Xx (xx%)	... ...	Xx (xx%)
VISIT4 (24 hours)	Same as above			
VISIT5 (48 hours)	Same as above			

A/0=Slight glazed appearance; B/1=marked glazed appearance; 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 site; H/3=Small petechial erosions and/or scabs

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Table 14.3.1.1
Summary of Treatment emergent Adverse Event by SOC and preferref term
Safety Population

Safety Population (N=xx)

SOC and Preferred Term	Serum A (N=XX)		Serum C...Saline (N=XX)...(N=XX)	Overall (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 AND SUBCUTANEOUS TISSUE DISORDERS	xx (xx.x)	xx	... ...	xx (xx.x)	xx
ERYTHEMA	xx (xx.x)	xx	... ...	xx (xx.x)	xx
DERMATITIS	xx (xx.x)	xx	... ...	xx (xx.x)	xx
GASTROINTESTINAL SYSTEM	xx (xx.x)	xx	... ...	xx (xx.x)	xx
ABDOMINAL PAIN	xx (xx.x)	xx	... ...	xx (xx.x)	xx
DRY MOUTH	xx (xx.x)	xx	... ...	xx (xx.x)	xx
VOMITTING	xx (xx.x)	xx		xx (xx.x)	xx

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

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Table 14.3.1.2
Summary of Treatment emergent Adverse Event by Severity
Safety Population

Safety Population (N=xx)

SOC and Preferred Term	Serum A (N=XX)						...	Overall (N=XX)					
	Mild		Moderate		Severe			Mild		Moderate		Severe	
	n (%)	nAE	n (%)	nAE	n (%)	nAE		n (%)	nAE	n (%)	nAE	n (%)	nAE
NUMBER OF SUBJECTS WITH AT LEAST ONE 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 AND SUBCUTANEOUS TISSUE DISORDERS	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	...	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
ERYTHEMA	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	...	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
DERMATITIS	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	...	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
GASTROINTESTINAL SYSTEM	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	...	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
ABDOMINAL PAIN	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	...	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
DRY MOUTH	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	...	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
VOMITTING	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	...	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx

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

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Listing 16.1.7
Randomisation information
Randomised Population

Subject Number	Age/Sex/Race[1]	Randomization Number	Test Site/Treatment Randomised	Date of randomization (dd/mmm/yyyy)
PPD				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.

PPD

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Listing 16.2.2
Individual Subjects Protocol Deviation
Randomised Population

Subject Number	Age/Sex/Race[1]	Visit	DeviationSequence	Protocol Deviation
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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Listing 16.2.7.1
All Adverse Events
Randomised Population
Treatment Group: Serum X

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

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

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PPD PPD

Programming Note for Listing 16.2.7.2:

- Repeat the same layout for listing 16.2.7.2
- Population should be used ‘Non randomised Subjects’
- The fourth column should be only ‘Start Date’
- Add footnote ‘Only SAEs are collected for non randomised subjects’
- Delete the footnote related to study day and adjust the numbers accordingly.