STATISTICAL ANALYSIS PLAN TEMPLATE

Statistical Analysis Plan
Version no. 1.0 – 20/03/2023

Clinical Investigation Plan Code FOLIAGE - 2022
EudraCT number NA

STATISTICAL ANALYSIS PLAN

Protocol Code: FOLIAGE - 2022
EudraCT number: NA

"CLINICAL AND INSTRUMENTAL EVALUATION OF THE FACE BIOREVITALIZATION EFFECT WITH THE MEDICAL DEVICE FOLIAGE HYDROFIL"

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APPROVAL

Protocol code: FOLIAGE - 2022

Title: CLINICAL AND INSTRUMENTAL EVALUATION OF THE FACE BIOREVITALIZATION EFFECT WITH THE MEDICAL DEVICE FOLIAGE HYDROFIL.

Document: Statistical Analysis Plan

Version No.: 1.0

Date: 20/03/2023

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LIST OF ABBREVIATIONS

AE	Adverse Event
ADE	Adverse Device Event
DM	Data Manager
DSMB	Data Safety Monitoring Board
eCRF	Electronic Case Report Form
FAS	Full Analysis Set
GAIS	Global Aesthetic Improvement Scale
ICH	International Conference of Harmonization
MedDRA	Medical Dictionary for Regulatory Activities
PAIS	Patient's Aesthetic Improvement Scale
PP	Per Protocol
PT	Preferred Term
SAF	Safety population
SAP	Statistical Analysis Plan
SOC	System Organ Class/Standard of Care
SOP	Standard Operating Procedure

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1. VERSION HISTORY

1.1 Version history of the SAP

Version Number	Summary/Reason for changes	Date issued
1.0	First version	20/03/2023

1.2 Version history of the Protocol

Version Number	Date	Description
1.0	02/02/2022	First version

1.3 Version history of the eCRF

Version Number	Date	Description
1.0	06/04/2022	First version in production

2. INTRODUCTION

This is a monocenter, open label post-market clinical follow-up investigation.

Each subject is treated with the study device Foliage Hydrofil.

Foliage Hydrofil is a CE marked, class III, resorbable medical device (sterile, non-pyrogenic and physiological gel) to be used for the hydration of the skin and for the correction of superficial skin imperfections of the face and body and in the process of repairing the dermal tissue.

This Statistical Analysis Plan has been designed to document the planned analyses that will be included in study reports.

It has been drawn in agreement with Latis srl internal SOP, and with ICH E6 (R2)1 and E9 guidelines (www.ich.org). The content of this SAP is based on the final version 1 of the clinical investigation plan dated 02/02/2022 and is reviewed by the Sponsor and finalized before the database lock.

3. STUDY OBJECTIVES

3.1 Primary Objectives

The primary objective of this clinical investigation is to evaluate and confirm the clinical performance of Foliage Hydrofil in the improvement of the skin hydration in the treated area at Day 98, from baseline.

3.2 Secondary Objectives

The secondary objectives of this clinical investigation are:

1. to evaluate the clinical performance of Foliage Hydrofil in the improvement of the skin hydration in the treated area at Day 21 and 42, from baseline;
2. to evaluate the improvement of the skin texture, skin tone, smoothing of fine lines and wrinkles in the treated area at Day 21, 42 and 98, from baseline;
3. to evaluate the aesthetic change from baseline as judged by the Investigator at Day 21, 42 and 98;
4. to evaluate the aesthetic change from baseline as judged by the subject at Day 21, 42 and 98;
5. to evaluate the subject's satisfaction at Day 21, 42 and 98.

4. STUDY METHODS

4.1 Study Design

This is a monocenter, open label post-market clinical follow-up investigation.

4.2 Treatment Administration

Each subject was treated with the study device.

The subject started treatment on the day (Day 1) after the first visit and received two further treatments at 3 weeks distance a part. Two months after the last treatment, a final visit has been planned to evaluate the final aesthetic result.

4.3 Randomization and Blinding

Not applicable: open-label clinical investigation.

5. STUDY ENDPOINTS

5.1 Primary Endpoints

The primary endpoint of the study is the change in skin hydration from baseline to Day 98, evaluated through corneometer skin examination.

5.2 Secondary Endpoints

Performance secondary endpoints of this clinical investigation are:

- the evaluation of the skin hydration from baseline to Day 21 and 42, through corneometer examination.

- the evaluation of the of the skin texture, skin tone, smoothing of fine lines and wrinkles from baseline in the treated area at Day 21, 42 and 98;
- the Investigator's aesthetic change assessment using the Global Aesthetic Improvement Scale (GAIS) at Day 21, 42 and 98. GAIS is a categorical scale with 5-points: worse than before treatment, no change, minimal improvement, good improvement, optimal improvement;
- the subject's aesthetic change assessment using the Patient's Aesthetic Improvement Scale (PAIS) at Day 21, 42 and 98. PAIS is a categorical scale with 5-points: worse, no change, somewhat improved, moderately improved, improved, very much improved;
- the evaluation of the overall subject's satisfaction of the treatment at Day 21, 42 and 98, through a 5-points scale: very much satisfied, satisfied, not satisfied nor unsatisfied, unsatisfied, very unsatisfied.

5.3 Safety Endpoints

Safety endpoints are the number, typology, severity of local and systemic adverse events. Particular attention will be paid to local adverse events like pain, erythema, edema, bruising.

6. PLANNED ANALYSIS

6.1 Interim Analysis

No interim analysis is planned.

6.2 Final Analysis

Final analysis will be performed according to the protocol and to this Statistical Analysis Plan, after data cleaning operations and DB Lock will be performed.

The statistical analysis will be performed using SAS 9.4 for Windows (SAS Institute Inc., Cary, NC, USA).

7. SAMPLE SIZE AND STATISTICAL POWER CONSIDERATION

It was assumed an average difference in the skin hydration evaluated through corneometer skin examination (capacitance) between baseline and Day 98 of 7.5, with a standard deviation of 8. With a statistically significant difference at an alpha = 0.05 a sample size of 20 subjects had 95% power to detect the above estimated difference Considering the above and a possible drop-out rate of 20%, 24 subjects have been recruited.

8. ANALYSIS POPULATIONS

8.1 Full Analysis set (FAS)

The Full Analysis set (FAS) will include all subjects of the SAF who have performed the baseline assessments and have at least one post-baseline assessment of any performance endpoint (primary or secondary).

8.2 Per-Protocol (PP) Population

The Per Protocol analysis set (PP) will include all subjects of the FAS who also meet all inclusion/exclusion criteria and who do not have any major protocol deviation.

8.3 Safety Population

The Safety analysis set (SAF) population will include all subjects enrolled who sign informed consent and receive at least one administration of the investigational device.

9. GENERAL ISSUES FOR STATISTICAL ANALYSIS

9.1 Definitions, Derived Variables and Datasets

Variable	Type	Description
corneo_before	Continous	Visit 1 (Day 1) – Capacitance Visit 2 (Day 21 ± 4 Days) – Capacitance Visit 3 (Day 42 ± 4 Days) – Capacitance
corneo	Continous	Visit 4 (Day 98 ± 7 Days) – Capacitance
texture_before	Discrete	Visit 1 (Day 1) – Skin texture Visit 2 (Day 21 ± 4 Days) – Skin texture Visit 3 (Day 42 ± 4 Days) – Skin texture 1 = Poor 2 = Good 3 = Very good
texture	Discrete	Visit 4 (Day 98 ± 7 Days) – Skin texture 1 = Poor 2 = Good 3 = Very good
finelines_before	Discrete	Visit 1 (Day 1) – Fine lines Visit 2 (Day 21 ± 4 Days) – Fine lines Visit 3 (Day 42 ± 4 Days) – Fine lines 1 = Poor 2 = Good 3 = Very good
finelines	Discrete	Visit 4 (Day 98 ± 7 Days) – Fine lines 1 = Poor 2 = Good 3 = Very good
tone_before	Discrete	Visit 1 (Day 1) – Skin tone Visit 2 (Day 21 ± 4 Days) – Skin tone

		Visit 3 (Day 42 ± 4 Days) – Skin tone 1 = Poor 2 = Sufficient 3 = Middle 4 = Good
tone	Discrete	Visit 4 (Day 98 ± 7 Days) – Skin tone 1 = Poor 2 = Sufficient 3 = Middle 4 = Good
wrinkles_before	Discrete	Visit 1 (Day 1) – Wrinkles Visit 2 (Day 21 ± 4 Days) – Wrinkles Visit 3 (Day 42 ± 4 Days) – Wrinkles 1 = Absent 2 = Slight 3 = Moderate 4 = Severe 5 = Extreme
wrinkles	Discrete	Visit 4 (Day 98 ± 7 Days) – Wrinkles 1 = Absent 2 = Slight 3 = Moderate 4 = Severe 5 = Extreme
qsorres_gais	Discrete	Visit 2 (Day 21 ± 4 Days) – Global aesthetic improvement scale (GAIS) by the Investigator Visit 3 (Day 42 ± 4 Days) – Global aesthetic improvement scale (GAIS) by the Investigator Visit 4 (Day 98 ± 7 Days) – Global aesthetic improvement scale (GAIS) by the Investigator 1 = Worse than before treatment 2 = No Change 3 = Minimal Improved 4 = Good Improved 5 = Optimal Improved
qsorres_pais	Discrete	Visit 2 (Day 21 ± 4 Days) – Patient's aesthetic improvement scale (PAIS) Visit 3 (Day 42 ± 4 Days) – Patient's aesthetic improvement scale (PAIS) Visit 4 (Day 98 ± 7 Days) – Patient's aesthetic improvement scale (PAIS)

		1 = Worse 2 = No Change 3 = Somewhat Improved 4 = Moderately Improved 5 = Very Much Improved 99 = Not done
qsorres_subjsatisf	Discrete	Visit 4 (Day 98 ± 7 Days) – Subject Overall Satisfaction 1 = Very Much Satisfied 2 = Satisfied 3 = Not satisfied nor unsatisfied 4 = Unsatisfied 5 = Very unsatisfied 99 = Not done

9.1.1 Baseline Values

Data collected at Visit 1 (Day 1), before any study treatment administration, will be considered as baseline values.

9.1.2 Duration of Exposure

The three-injection treatment session were scheduled at Visit 1 (Day 1), Visit 2 (Day 21 ±4 days) and Visit 3 (42 ± 4 days). A Follow up visit (Visit 4) was scheduled at days 98 ±7 days.

The extent of exposure will be estimated based on the treatment duration.

9.1.3 Treatment Compliance

Not applicable. The administrations of the investigational medical device were performed at the investigational site by a qualified professional experienced in administering injections, who was assure the correctness of subject compliance.

9.1.4 Methods for Withdrawals and Missing Data

Missing data will not be replaced in any statistical analysis.

9.2 Multicenter Studies Considerations

Not applicable; this is a single-center study.

9.3 Multiple Comparisons and Multiplicity

No adjustment is needed.

9.4 Data Safety Monitoring Board (DSMB)

No DSMB was established for this study.

10. STUDY SUBJECTS

10.1 Disposition of Subjects

Subjects' disposition by study visit will be described and summarized in the Table 1.1. Reasons for withdrawal will be described.

10.2 Protocol Deviations

Protocol deviations will be reviewed and discussed with the sponsor before the database lock. Statisticians and DM will also review protocol deviations in order to define the datasets prior the database lock.

Protocol deviations will be described in the Table 1.2 and in the Listing 2.

11. EFFICACY ANALYSIS

11.1 Analysis datasets

The analysis of safety endpoints will be performed on the SAF population. Analysis of performance endpoints will be performed on the FAS population. Additionally, analysis of primary endpoint will also be performed on the PPAS population.

11.2 Demographics and Baseline Characteristics

Demographic (gender, age) and baseline characteristics (medical and surgical history, skin and physical examination) will be summarized from Table 1.3 to Table 1.6 and from Listing 4.1 to Listing 4.4.

If the Safety population will be much bigger than FAS population, the analysis of demographic and baseline characteristics will be repeated on the FAS population.

The descriptive statistics will include number of observations, mean, standard deviation, median, minimum and maximum for continuous variables and number of observations and their percentages for categorical parameters.

11.3 Measurements of Treatment Compliance

Not applicable.

11.4 Efficacy Analysis

11.4.1 Primary Efficacy Endpoints

Paired t-test, when the skin hydration is normally distributed, or the corresponding non-parametric Wilcoxon signed rank test will be used to assess a significant change in skin hydration, evaluated through corneometer skin examination (capacitance), from baseline to Day 98.

The primary endpoint will be described in the Table 2.1.1.

11.4.2 Secondary Efficacy Endpoints

Paired t-test, when the skin hydration is normally distributed, or the corresponding non-parametric Wilcoxon signed rank test will be used to assess a significant change in skin hydration, evaluated through corneometer skin examination (capacitance), from baseline to Day 21 and Day 42.

Subjects will be considered responders when skin hydration increase is at least 7,5 between baseline and Day 98 and non-responders when there is not any increase in skin hydration. The number (N) and proportion of subjects (%) for each category will be reported.

The skin texture, skin tone, smoothing of fine lines and wrinkles will be summarized at all time-points in terms of number (N) and percentage (%).

Subjects will be considered responders when Investigator's evaluation of skin texture, skin tone and smoothing of fine lines increases at least one category on the assessment scale, from baseline; otherwise, subjects will be considered non-responders.

Subjects will be considered responders when Investigator's evaluation of wrinkles decreases at least two grades on the severity rating scale, from baseline; otherwise, subjects will be considered non-responders.

Subjects whose grade on the severity rating scale of Investigator's evaluation of wrinkles decreases from 2 "Slight" to 1 "Absent" will also be considered responders.

The Global Aesthetic Improvement Scale (GAIS) filled-in by the investigator and the Patient's Aesthetic Improvement Scale (PAIS) filled-in by the subject will be summarized at all time-points in terms of number (N) and percentage (%).

The overall subject's evaluation of satisfaction with the treatment at Day 98, performed by means of the 5-item scale, will be summarized through number (N) and proportion of subjects (%) for each item.

The secondary endpoints will be described from Table 2.2.1 to Table 2.2.7.

11.5 Summary of Efficacy Analyses

Endpoint	Analysis	Populations
Change from baseline (Visit 1) to day 98 (Visit 4) of the skin hydration	Paired Student's t-test/ Wilcoxon signed-rank test	*FAS* *PP*
Change from baseline (Visit 1) to day 21 (Visit 2) of the skin hydration	Paired Student's t-test/ Wilcoxon signed-rank test	*FAS*

Change from baseline (Visit 1) to day 42 (Visit 3) of the skin hydration	Paired Student's t-test/ Wilcoxon signed-rank test	*FAS*
Percentage of subjects improved (Responders) on skin hydration at Day 98 (Visit 4) in comparison to the baseline visit	Number (N) and the proportion of subjects (%) for each item	*FAS*
Percentage of subjects improved (Responders) on Investigator's Evaluation of skin texture, skin tone, smoothing of the fine lines and wrinkles at each time point (Visit 2, Visit 3 and Visit 4) in comparison to the baseline visit	Number (N) and the proportion of subjects (%) for each item	*FAS*
Percentage of subjects improved on the Global Aesthetic Improvement Scale (GAIS) at each time point (Visit 2, Visit 3 and Visit 4) in comparison to the baseline visit	Number (N) and the proportion of subjects (%) for each item	*FAS*
Percentage of subjects improved on the Patient's Aesthetic Improvement Scale (PAIS) at each time point (Visit 2, Visit 3 and Visit 4) in comparison to the baseline visit	Number (N) and the proportion of subjects (%) for each item	*FAS*
Subject's Evaluation of satisfaction with the treatment at Day 98 (Visit 4) by means of a 5-items scale	Number (N) and the proportion of subjects (%) for each item	*FAS*

12. SAFETY EVALUATION

12.1 Extent of Exposure

The extent of exposure is 42 (± 4) days.

12.2 Adverse Events

All enrolled subjects receiving at least one treatment injection will be included in the safety analysis.

Adverse events (AEs) and Adverse Device Events (ADEs) will be coded using the last updated version of the Medical Dictionary for Regulatory Activities (MedDRA) dictionary to give a preferred term (PT) and a system/organ class term (SOC) for each event. The number of subjects who experienced at least one AE or ADE,

study product-related AE or ADE, serious AE or ADE, severe AE or ADE and the number of subjects withdrawn due to AE will be summarized in the Table 3.1.

For each SOC and preferred term, summaries will be made with respect to the proportion of subjects having at least one occurrence of that event during the study and the total number of events. The incidence of AEs and ADEs will be presented overall, by SOC and preferred term, and additional grouping by severity and relationship to the study treatment in the Table 3.2. Local tolerability at the site of administration will be carefully considered.

All Adverse Events will be described in the Listing 7.

13. DEVIATIONS FROM THE PROTOCOL SPECIFIED ANALYSIS

Waiting for EC approval (more than 6 months, due to Ethics Committee organization and procedures) and therefore for the start of the study, the centre purchased a new corneometer (fitted with an integrated sensor - average 50), with a capacitance algorithm based on a different scale from the one assumed when drafting the protocol.

The scale of the new corneometer is based on lower numbers, with normal values around 50 rather than around 100.

Therefore, after discussions with Dr. Lazzari, it was decided that for skin hydration at corneometer, the subjects can be considering responders to the treatment when skin hydration increase is at least 7,5 from baseline to Day 98, using an absolute evaluation, instead of a percentage as hypothesized in the protocol drafting phase.

About the inclusion criterion n. 4 "Corneometer Capacitance of the area treated $\leq$ 80", Dr. Lazzari declares that the capacitance = 45 at new corneometer can be consider equivalent to capacitance = 80 at previous corneometer.

No other changes from the details specified in the study protocol have been included in this Statistical Analysis Plan (SAP).

14. LIST AND SAMPLES OF TABLES, FIGURES AND GRAPHS

The following lists of tables might not be exhaustive. Additional tables can be produced if necessary.

14.1 Demographic data

Table 1.1 Subjects' disposition (Safety population)

Table 1.2 Protocol deviations (Safety population)

Table 1.3 Demographic characteristics (Safety population)

Table 1.4 Medical history (Safety population)

Table 1.5 Surgical history (Safety population)

Table 1.6 Skin and physical examination (Safety population)

14.2 Efficacy data

14.2.1 Primary endpoints

Table 2.1.1 Change from baseline (Visit 1) to day 98 (Visit 4) of the skin hydration, evaluated through corneometer skin examination (FAS Population)

Table 2.1.2 Change from baseline (Visit 1) to day 98 (Visit 4) of the skin hydration, evaluated through corneometer skin examination (PP Population)

14.2.2 Secondary endpoints

Table 2.2.1 Change from baseline (Visit 1) to day 21 (Visit 2) of the skin hydration, evaluated through corneometer skin examination (FAS Population)

Table 2.2.2 Change from baseline (Visit 1) to day 42 (Visit 3) of the skin hydration, evaluated through corneometer skin examination (FAS Population)

Table 2.2.3 Percentage of subjects improved (Responders) on skin hydration, evaluated through corneometer skin examination, at Day 98 (Visit 4) in comparison to the baseline visit (FAS Population)

Table 2.2.4 Percentage of subjects improved (Responders) on Investigator's Evaluation of skin texture, skin tone, smoothing of the fine lines and wrinkles at each time point (Visit 2, Visit 3 and Visit 4) in comparison to the baseline visit (FAS Population)

Table 2.2.5 Percentage of subjects improved on the Global Aesthetic Improvement Scale (GAIS) at each time point (Visit 2, Visit 3 and Visit 4) in comparison to the baseline visit (FAS Population)

Table 2.2.6 Percentage of subjects improved on the Patient's Aesthetic Improvement Scale (PAIS) at each time point (Visit 2, Visit 3 and Visit 4) in comparison to the baseline visit (FAS Population)

Table 2.2.7 Subject's Evaluation of satisfaction with the treatment at Day 98 (Visit 4) by means of a 5-items scale (FAS Population)

14.3 Safety data

Table 3.1 Analysis of adverse events observed (Safety population)

Table 3.2 Display of adverse events observed (Safety population)

14.4 Sample tables

Tables reporting statistical analysis will be issued as PDF files. Mock samples are reported in the following sections.

14.4.1 Sample summary table

Sponsor: Phitogen Holding S.p.A. Page 1 of x
Protocol FOLIAGE - 2022

Table xx.x.x
(..... Population)

Characteristic	Statistic	Foliage Hydrofil
VAR 1	Class A	xx (xx.x%)
	Class B	xx (xx.x%)
VAR 2	N	xx
	Mean (SD)	xx.xx (xx.xx)
	Median	xx.xx
	Min - Max	xx.xx / xx.xx
VAR 3	Class A	xx (xx.x%)
	Class B	xx (xx.x%)
	Class C	xx (xx.x%)
	Class D	xx (xx.x%)
VAR 4	N	xx
	Mean (SD)	xxx.xx (x.xx)
	Median	xxx.xx
	Min - Max	xxx.xx / xxx.x
VAR 5	N	xx
	Mean (SD)	xx.xx (xx.xx)
	Median	xx.xx
	Min - Max	xx.xx / xxx.xx
VAR 6	N	xx
	Mean (SD)	xx.xx (x.xx)
	Median	xx.xx
	Min - Max	xx.xx / xx.xx

Note: ... ...

Program: Txxxxxx xx.sas CONFIDENTIAL Date: xxXXXxxxx

14.4.2 Sample table for efficacy analysis – continuous variables

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Protocol FOLIAGE - 2022

Table xx.x.x.x
(…. Population)

Endpoint	Statistic	Foliage Hydrofil
Visit 1 (Baseline)	N	xxx
	Mean (SD)	-x.xx (x.xx)
	Median	-x.xx
	Min - Max	-x.xx / x.xx
Visit 2	N	xxx
	Mean (SD)	-x.xx (x.xx)
	Median	-x.xx
	Min - Max	-x.xx / x.xx
	p-value	x.xxx
Visit 3	N	xxx
	Mean (SD)	-x.xx (x.xx)
	Median	-x.xx
	Min - Max	-x.xx / x.xx
	p-value	x.xxx
Visit 4 (End of study)	N	xxx
	Mean (SD)	-x.xx (x.xx)
	Median	-x.xx
	Min - Max	-x.xx / x.xx
	p-value	x.xxx

Statistical significance: * p<0.05

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14.4.3 Sample table for efficacy analysis – discrete variables

Sponsor: Phitogen Holding S.p.A. Page 1 of x
Protocol FOLIAGE - 2022

Table xx.x.x.x
(..... Population)

Characteristic	Statistic	Foliage Hydrofil
Visit 1 (Baseline)	Class A	xx (xx.x%)
	Class B	xx (xx.x%)
Visit 2	Class A	xx (xx.x%)
	Class B	xx (xx.x%)
	p-value	x.xxx
Visit 3	Class A	xx (xx.x%)
	Class B	xx (xx.x%)
	p-value	x.xxx
Visit 4 (End of study)	Class A	xx (xx.x%)
	Class B	xx (xx.x%)
	p-value	x.xxx

Statistical significance: * p<0.05

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14.4.4 Sample table for adverse events analysis

Sponsor: Phitogen Holding S.p.A. Page 1 of x
Protocol FOLIAGE - 2022

Table xx.x.x.x
Analysis of adverse events observed
(Safety Population)

AE details	Statistic	Foliage Hydrofil
Have any AE occurred?	NO	x (xx.x%)
	YES	x (xx.x%)
Total number of adverse events	N	(N=xxx)
Relatedness with study treatment	Certain	x (xx.x%)
	Probable	x (xx.x%)
	Possible	x (xx.x%)
	Doubtful	x (xx.x%)
	None	x (xx.x%)
	Unknown	
Severity	Grade 1 (Mild)	x (xx.x%)
	Grade 2 (Moderate)	x (xx.x%)
	Grade 3 (Severe)	x (xx.x%)
	Grade 4 (Life-threatening consequences)	
	Grade 5	
Seriousness	YES	x (xx.x%)
	NO	x (xx.x%)

Statistical significance: * p<0.05

Program: Txxxxxxxx xxx.sas CONFIDENTIAL Date: xxXXxxxx

14.4.5 Sample table for adverse events display

Sponsor: Phitogen Holding S.p.A. Page 1 of x
Protocol FOLIAGE - 2022

Table xx.x.x.x
Display of adverse events observed
(Safety Population)

	Foliage Hydrofil		
System Organ Class (SOC) - Preferred Term (PT)	Event	Patients	(%)
OVERALL	x	x	x.xx
SOC 1	x	x	x.xx
- PT 1	x	x	x.xx
- PT 2	x	x	x.xx
- PT 3	x	x	x.xx
SOC 1	x	x	x.xx
- PT 1	x	x	x.xx
- PT 2	x	x	x.xx
- PT 3	x	x	x.xx
SOC 1	x	x	x.xx
- PT 1	x	x	x.xx
- PT 2	x	x	x.xx
- PT 3	x	x	x.xx
SOC 1	x	x	x.xx
- PT 1	x	x	x.xx
- PT 2	x	x	x.xx
- PT 3	x	x	x.xx
SOC 1	x	x	x.xx
- PT 1	x	x	x.xx
- PT 2	x	x	x.xx
- PT 3	x	x	x.xx
SOC 1	x	x	x.xx
- PT 1	x	x	x.xx
- PT 2	x	x	x.xx
- PT 3	x	x	x.xx
SOC 1	x	x	x.xx
- PT 1	x	x	x.xx
- PT 2	x	x	x.xx
- PT 3	x	x	x.xx

Program: Txxxxxxxx xxx.sas CONFIDENTIAL Date: xxXXXxxxx

15. REFERENCES

None.

16. APPENDICES

16.1 Study information

Study information appendices will be attached to the CIR.

16.2 List and samples of Subject Data Listings

The following list of listings might not be exhaustive. Additional listings can be produced if necessary.

The following data listings will be attached to the CIR:

Listing 1 Discontinued subjects

Listing 2 Protocol deviations

Listing 3 Subjects excluded from the efficacy analysis

Listing 4.1 Demographic data

Listing 4.2 Medical history

Listing 4.3 Surgical history

Listing 4.4 Skin and physical examination

Listing 5.1 Individual efficacy response data – skin hydration at each time point (Visit 1, Visit 2, Visit 3 and Visit 4)

Listing 5.2 Individual efficacy response data – skin surface characteristics at each time point (Visit 1, Visit 2, Visit 3 and Visit 4)

Listing 5.3 Individual efficacy response data – Global Aesthetic Improvement Scale (GAIS) by the investigator at each time point (Visit 2, Visit 3 and Visit 4)

Listing 5.4 Individual efficacy response data – Patient's Aesthetic Improvement Scale (PAIS) at each time point (Visit 2, Visit 3 and Visit 4)

Listing 5.5 Individual efficacy response data – subject overall satisfaction at Day 98 (Visit 4)

Listing 6 Adverse events

Listing 7 Concomitant medications

16.2.1 Sample listing

Listings will be issued as PDF files. Mock listings are reported in the following section.

Sponsor: Phitogen Holding S.p.A. Page 1 of x
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Listing xx.x.x.x

SUBJECT	VISIT	VAR 1	VAR 2	VAR 3	VAR 4	VAR 5	VAR 6	VAR 7	VAR 8	VAR 9	VAR 10	VAR 11	VAR 12	VAR 13
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	x	x	x	x.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	x.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	xx.x	xx	xx	xx	xx.x	-x.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	x.x	xx	xx	xx	xx.x	x.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-x.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	x.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	x.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xxx	xx.x	xx	xx	xx	xx.x	-x.x	xx	xx	xx	xx.x	x.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	xx.x	xx	xx	xx	xx.x	x.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	x.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	xx	x	x	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-x.x	xx	xx	xx	xx.x	-x.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	x	x	x	x.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	x.x	xx	xx	xx	xx.x	-x.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-x.x	xx	xx	xx	xx.x	-x.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-x.x					
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-x.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-x.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	xx	xx	xx	xx.x	-x.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xxx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-x.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	xx	x	x	x.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-x.x	xx	x	x	x.x	-xx.x

Program: Lxxxxxxxx.sas CONFIDENTIAL Date: xxXXXxxxx