STATISTICAL ANALYSIS PLAN

Protocol Code: ReGl/20/Dec-Der/001
EudraCT number: NA

"MULTICENTER, OPEN LABEL, UNCONTROLLED CLINICAL INVESTIGATION ON THE PERFORMANCE AND SAFETY OF DERMORELIZEMA ECOFOAM IN THE MANAGEMENT OF SOME DERMATITIS IN THE ADULT"

Sponsor
Relife S.r.l.
Via dei Sette Santi 3
50131 Florence, ITALY
Phone: +39 055 56809345
Fax: +39 055 56809346

Contract Research Organization
Latis Srl
Viale Sauli, 39/5 - 16121 Genoa - Italy
Phone: +39 010 562234
Fax: +39 010 540699

APPROVAL

Protocol code: ReGI/20/Dec-Der/001

Title: MULTICENTER, OPEN LABEL, UNCONTROLLED CLINICAL INVESTIGATION ON THE PERFORMANCE AND SAFETY OF DERMORELIZEMA ECOFOAM IN THE MANAGEMENT OF SOME DERMATITIS IN THE ADULT

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Author:

Statistician, Latis Srl

Name and Surname CAMILLA PALERMITI

Signature _____ Date 10 / 06 / 2022

Approval:

Scientific Director, Latis Srl

Name and Surname LAURA MICHELLINI

Signature _____ Date 10 / 06 / 2022

Sponsor's Representative

Name and Surname SILVIA INNOCENTI (HSA)

Signature _____ Date 10 / 06 / 2022

Name and Surname MARTINA MANNI (SME)

Signature _____ Date 10 / 06 / 2022

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

ADE	Adverse Device Effect
AE	Adverse Event
CIP	Clinical Investigation Plan
CRF	Case Report Form
DLQI	Dermatology Life Quality Index questionnaire
DSMB	Data Safety Monitoring Board
EASI	Eczema Area and Severity Index
eCRF	Electronic Case Report Form
FAS	Full Analysis Set
IFU	Instructions For Use
IGA	Investigator Global Assessment
IEC	Indipendent Ethics Committee
MedDRA	Medical Dictionary for Regulatory Activities
PP	Per-Protocol
PT	Preferred Term
QoL	Quality of Life
SAP	Statistical Analysis Plan
SOC	System Organ Class
VAS	Visual Analogue Scale

1. VERSION HISTORY

1.1 Version history of the SAP

Version Number	Summary/Reason for changes	Date issued
1.0	First version	10/06/2022

1.2 Version history of the Protocol

Version Number	Date	Description
1.0	06/11/2020	First version submitted

1.3 Version history of the eCRF

Version Number	Date	Description
1.0.0	12/03/2021	First deployment

2. INTRODUCTION

DermoRelizema ecofoam is a topical compact mousse indicated for treatment of the signs and symptoms associated with all types of dermatitis (including atopic, contact dermatitis, dermatitis caused by radiotherapy and by sun radiations) and erythema. The mechanism of action of DermoRelizema ecofoam is based on the creation of a protective thin layer on the skin, which protects the skin against external irritants without hindering normal transpiration. It helps reducing skin redness and its derma-protective action it helps maintaining and restoring the physiological skin barrier. Thanks to its light texture, it can be easily applied on wide areas.

DermoRelizema ecofoam is a CE marked medical device class IIa, manufactured by Relife Srl, that is the Sponsor of this post-market clinical follow-up investigation.

In this clinical investigation DermoRelizema ecofoam will be used to treat and alleviate dermatitis severity and symptoms as perceived by the patients, in compliance with its Instructions for Use (IFU). Different typologies of skin conditions will be treated like atopic dermatitis, irritant dermatitis, contact dermatitis, as they have common symptomatology and they all could benefit from the treatment with the topic product under investigation.

Dermatitis is a skin inflammatory disease commonly spreading in a limited area of the body and characterized by reddening, itching and skin dryness of the affected epidermis. Dermatitis is a condition that can interfere with social function, sleep and employment. Its persistence and accompanying pruritus may be stressful and frustrating for patients.

The most common types of dermatitis are contact dermatitis (CD) and atopic dermatitis (AD), also referred as atopic eczema, but also dermatitis caused by radiotherapy or solar radiations can occur. Only atopic dermatitis and contact dermatitis will be included in this clinical investigation.

DermoRelizema ecofoam (DLP034) CE mark was supported by literature research. In order to allow the Manufacturer, Relife Srl, to review and confirm the clinical performance and safety of the medical device DermoRelizema ecofoam in the post-market phase, this post-market clinical follow-up investigation was designed and is going to be conducted in adult males and females affected by mild to moderate dermatoses, like AD, ICD or ACD.

3. STUDY OBJECTIVES

3.1 Primary Objective

The primary objective of this clinical investigation is to evaluate and confirm the performance of the DermoRelizema ecofoam medical device in the improvement of the dermatitis severity, by alleviating the symptomatology.

The disease severity was clinically measured through the Investigator Global Assessment (IGA) for dermatitis after 28 days of treatment.

3.2 Secondary Objectives

The secondary objectives of this clinical investigation are:

1. to evaluate the performance of DermoRelizema ecofoam in the improvement of dermatitis severity (IGA) after 14 and 42 days of treatment;
2. to evaluate the eczema improvement through the EASI (Eczema Area and Severity Index) score;
3. to evaluate the improvement in itching, burning, pain and pruritus at visits, as reported by the subject at visits by VAS;
4. to evaluate improvement in the Quality of Life (QoL) of the subject related to his/her dermatitis, through the DLQI (Dermatology Life Quality Index) questionnaire;
5. to evaluate the subject's adherence to treatment.
6. to evaluate the subject's and Investigator's global evaluation of performance of DermoRelizema ecofoam;
7. to evaluate the subject's overall acceptability of DermoRelizema ecofoam.

4. STUDY METHODS

4.1 Study Design

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

All the subjects were allocated to the following treatment group:

- DermoRelizema ecofoam, topically applied twice a day in all the affected areas for 42 consecutive days.

The subject started treatment on the first day of study and continued until 42 days after the first application. The treatment may have been prolonged or shortened of maximum 2 days, in the case intermediate and/or final visits were delayed.

4.2 Treatment Administration

Patients were instructed to use DermoRelizema ecofoam two times daily: the first application in the morning and the second in the evening before bedtime, for 42 consecutive days.

At the first use of the product the patient were instructed to press the valve two or three times to activate the pump mechanism. After this, the subject pressed the valve gently to obtain one or more doses of the product to apply on the selected area and massage.

4.3 Randomization and Blinding

Not applicable: open-label clinical investigation.

5. STUDY ENDPOINTS

5.1 Primary Endpoint

Change from baseline (Visit 1) to day 28 (Visit 3) in Investigator Global Assessment (IGA). The assessment will be also dichotomized in terms of treatment success or treatment failure.

5.2 Secondary Endpoints

Secondary endpoints are:

1. Change from baseline (Visit 1) to day 14 (Visit 2) and day 42 (Visit 4) in Investigator Global Assessment (IGA). The assessment will be also dichotomized in terms of treatment success or treatment failure and described using Number (N) and the proportion of patient (%).
2. Change from baseline (Visit 1) to each time point (day 14, day 28 and day 42) in EASI (Eczema Area and Severity Index) score.
3. Change from baseline (Visit 1) to each time point (day 14, day 28 and day 42) in DLQI (Dermatology Life Quality Index) score.
4. Change from baseline (Visit 1) to each time point (day 14, day 28 and day 42) in itching, burning, pain and pruritus, as reported by the subject by VAS.
5. The subject's adherence to treatment (number of applications reported on the subject's diary).
6. The subject's and Investigator's global evaluation of performance of DermoRelizema ecofoam, through a specific questionnaire. The variable will be also dichotomized in terms of improved/not improved.
7. To evaluate the subject's overall acceptability of DermoRelizema ecofoam, through a specific questionnaire.

5.3 Safety Endpoints

To evaluate the local and general tolerability of DermoRelizema ecofoam. Adverse events and adverse device events were recorded and evaluated.

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

An exact binomial test with a nominal 5% two-sided significance level has 80% power to detect the difference between the Null hypothesis proportion, π_0 of 0.5 (i.e., 50% of patients with treatment success) and the alternative proportion, π_1, of 0.75 (i.e., 75% of patients with treatment success) when the sample size is 30 subjects. Assuming a possible 25% dropout rate, 40 subjects were enrolled, according to the CIP provisions.

8. ANALYSIS POPULATIONS

8.1 Full Analysis Set (FAS)

The FAS population includes all subjects of the safety population who have performed the baseline assessments and had at least one post-baseline assessment of any performance endpoint (primary or secondary).

8.2 Per-Protocol (PP) Population

The PP population includes all subjects of the FAS who also met all inclusion/exclusion criteria and who did not have any major protocol deviation.

8.3 Safety Population

The Safety Population includes all the subjects enrolled who signed informed consent and received at least one administration of the investigational device.

9. GENERAL ISSUES FOR STATISTICAL ANALYSIS

9.1 Definitions, Derived Variables and Datasets

Variable	Type	Description
qsorres_iga	Discrete	Investigator's global assessment: 0 = Clear 1 = Almost clear 2 = Mild 3 = Moderate 4 = Severe 5 = Very severe
qsorres_easi	Continous	EASI Score
qsorres_dlqi	Continous	DLQI score
qsorres_vas_pain	Continous	VAS for pain rating

qsorres_vas_itch	Continous	VAS for itching rating
qsorres_vas_burn	Continous	VAS for burning rating
qsorres_vas_prur	Continous	VAS for pruritus rating
ecdos_skipped	Continous	Treatment skipped applications
ecdosfrq	Continous	Treatment performed applications
qsorres_su_perf	Discrete	Subject's global evaluation of performance: 1 = Very much improved 2 = Improved 3 = Minimally improved 4 = No change 5 = Minimally worse 6 = Worse 7 = Very much worse
qsorres_inv_perf	Discrete	Investigator's global evaluation of performance: 1 = Very much improved 2 = Improved 3 = Minimally improved 4 = No change 5 = Minimally worse 6 = Worse 7 = Very much worse
qsorres_su_sat	Discrete	Subject's overall acceptability – Pleasant feeling with product: 1 = Very much satisfied 2 = Satisfied 3 = Neither satisfied nor dissatisfied 4 = Dissatisfied 5 = Very much dissatisfied

9.1.1 Baseline Values

Data and Measures collected at Visit 1, before any study treatment administration, are considered as baseline values.

9.1.2 Duration of Exposure

The planned treatment duration was of 1,5 month (42 days ±2).

9.1.3 Treatment Compliance

The Investigator was responsible for ensuring the accountability of the study product.

The Investigator should maintain records that adequately documented:

- that the subjects were provided with the quantities specified by the clinical investigation plan/amendment(s)
- that all study products provided by the Sponsor were fully reconciled.

The investigator visually checked the empty/unused/partially used tubes of study product returned by the subjects at study visit. In order to quantify the compliance to the treatment the Investigator also asked to the subject if the product was used according to the instructions, how many times the treatment was skipped and how many study product applications were performed, according to subject's diary. The subject will be considered compliant to the treatment if the number of skipped applications is not exceeding 20% of the expected applications (i.e. the compliance of a compliant subject should be between 80% e 120%).

In the Listing 16.2.5, adherence to treatment will be described.

9.1.4 Methods for Withdrawals and Missing Data

Missing data will not be replaced in any statistical analysis.

9.2 Multicenter Studies Considerations

No covariates or interaction analysis will be performed.

9.3 Multiple Comparisons and Multiplicity

This is a single-arm clinical investigation and no adjustment for multiplicity will be used.

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 14.1.1. Reasons for withdrawal will be described.

10.2 Protocol Deviations

Protocol deviations will be reviewed and discussed with the sponsor before the database lock during Data Review Meeting.

Protocol deviations will be summarized in the Table 14.1.2 and described in the Listing 16.2.2.

11. EFFICACY ANALYSIS

11.1 Analysis datasets

The analysis of safety endpoints will be performed on the Safety population. Analysis of performance endpoints will be performed on the FAS population. The analysis of primary endpoint will be repeated in the Per-Protocol population.

11.2 Demographics and Baseline Characteristics

Demographic (gender, age) and baseline characteristics will be summarized in the Tables 14.1.3 and 14.1.4. Medical history and surgical history will be summarized in the Tables 14.1.5 and 14.1.6.

From Listing 16.2.4.1 to Listing 16.2.4.4, all demographic and baseline characteristics will be described.

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

Treatment compliance will be assessed through the counting of the number of performed applications, according to the subject's diary and through the counting of the number of planned applications.

The number of performed applications will be recorded on the eCRF separately for the three study periods: Visit 1 – Visit 2, Visit 2 – Visit 3 and Visit 3 – Visit 4. The total number of performed applications will be the sum of the performed applications of the three study periods. The total number of planned applications will be estimated based on the treatment duration x 2 times.

To calculate the treatment compliance, the following formula will be used:

$$\frac{Total\ number\ of\ performed\ applications}{Total\ number\ of\ planned\ applications} * 100$$

Treatment compliance will be described in Listing 16.2.5.

11.4 Efficacy Analysis

11.4.1 Primary Efficacy Endpoints

Wilcoxon signed-rank test will be used to assess a significant change in Investigator Global Assessment (IGA) from baseline (Visit 1) to day 28 (Visit 3). The assessment will be also dichotomized in terms of treatment success (decrease in IGA between baseline and day 28 $\geq$ 1) or treatment failure (no decrease in IGA, i.e. IGA at day 28 equal to or higher than IGA at baseline). It will be described using number (N) and the proportion of subjects (%) in the Tables 14.2.1.1 and 14.2.1.2. The proportion of treatment successes will be compared to a referent proportion (50%, Null hypothesis proportion) using the exact binomial test.

11.4.2 Secondary Efficacy Endpoints

Wilcoxon signed-rank test will be used to assess a significant change in Investigator Global Assessment (IGA) from baseline (Visit 1) to day 14 (Visit 2) and day 42 (Visit 4). The assessment will be also dichotomized in terms of treatment success (score decrease $\geq$ 1) or treatment failure (no score decrease). It will be described using number (N) and the proportion of subjects (%). The proportion of treatment successes will be compared to a referent proportion (50%, Null hypothesis proportion) using the exact binomial test.

Changes from baseline (Visit 1) to 14 days (Visit 2), 28 days (Visit 3) and 42 days (Visit 4) of treatment in EASI score, DLQI score and VAS for pruritus, itching, burning and pain severity will be analyzed using paired Student's t-test (or Wilcoxon signed-rank test if the variable is not normally distributed).

The number of applications reported on the subject's diary will be used to evaluate adherence to treatment. Treatment compliance will be summarized by the number of patients (N), mean, standard deviation, median, minimum, maximum.

Subject's and Investigator's global evaluation of performance of the study product obtained at the end of the study (Visit 4) by means of a 7-items scale will be summarized through number (N) and proportion of subjects (%) for each item. The variable will be also dichotomized in terms of improved (1=Very much improved or 2=Improved or 3=Minimally improved) or not improved (4=No change or 5=Minimally worse or 6=Worse or 7=Very much worse).

Subject's evaluation of overall acceptability with treatment, obtained by means of a 5-item scale will be summarized through number (N) and the proportion of subjects (%) for each item.

The secondary endpoints will be described from Table 14.2.2.1 to Table 14.2.2.8.

11.5 Summary of Efficacy Analyses

Endpoint	Analysis	Populations
Change from baseline (Visit 1) to day 28 (Visit 3) in Investigator Global Assessment (IGA). Proportion of treatment successes at Visit 3.	Wilcoxon signed rank-test Exact binomial test	*FAS* *PP*
Change from baseline (Visit 1) to day 14 (Visit 2) and day 42 (Visit 4) in Investigator Global Assessment (IGA). Proportion of treatment successes at Visit 2 and Visit 4.	Wilcoxon signed rank-test Exact binomial test	*FAS*
Change from baseline (Visit 1) to each time point (Visit 2, Visit 3 and Visit 4) in EASI (Eczema Area and Severity Index) score	Paired Student's t-test/ Wilcoxon signed-rank test	*FAS*
Change from baseline (Visit 1) to each time point (Visit 2, Visit 3 and Visit 4) in DLQI (Dermatology Life Quality Index) score	Paired Student's t-test/ Wilcoxon signed-rank test	*FAS*
Change from baseline (Visit 1) to each time point (Visit 2, Visit 3 and Visit 4) in itching, burning, pain and pruritus, as reported by the subject by VAS	Paired Student's t-test/ Wilcoxon signed-rank test	*FAS*
Subject's adherence to treatment.	Number (N), mean, SD, median, minimum and maximum	*FAS*
Subject's and Investigator's global evaluation on performance of the study product at the end of the study (Visit 4) by means of a 7-items scale (the variable will be also dichotomized in terms of improved or not improved).	Number (N) and the proportion of subjects (%) for each item	*FAS*

Subject's overall acceptability of the treatment at the end of the study (Visit 4) by means of a 5-item 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 1,5 month (42 days ±2).

12.2 Adverse Events

All enrolled subjects receiving at least one treatment application will be included in the safety analysis. The safety analysis will include Deaths, Serious Adverse Events and other significant Adverse Events.

Adverse events (AEs) and Adverse Device Events (ADEs) will be coded using the 25.0 version of the Medical Dictionary for Regulatory Activities (MedDRA) 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 14.3.1.

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 14.3.2. Local tolerability at the site of administration (e.g., skin increased itching or redness or irritation) will be carefully considered.

Adverse events will be fully reported in Listing 16.2.7.

12.3 Other safety endpoints

None.

13. DEVIATIONS FROM THE PROTOCOL SPECIFIED ANALYSIS

No deviation from the analyses 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 14.1.1 Subjects' disposition (Safety population)

Table 14.1.2 Protocol deviations (Safety population)

Table 14.1.3 Demographic characteristics (FAS population)

Table 14.1.4 Disease details at baseline (FAS population)

Table 14.1.5 Medical history (FAS population)

Table 14.1.6 Surgical history (FAS population)

14.2 Efficacy data

14.2.1 Primary endpoints

Table 14.2.1.1 Change from baseline (Visit 1) to day 28 (Visit 3) in Investigator Global Assessment (IGA) (FAS Population)

Table 14.2.1.2 Proportion of treatment successes at Visit 3 (FAS Population)

Table 14.2.1.3 Change from baseline (Visit 1) to day 28 (Visit 3) in Investigator Global Assessment (IGA) (PP Population)

Table 14.2.1.4 Proportion of treatment successes at Visit 3 (PP Population)

14.2.2 Secondary endpoints

Table 14.2.2.1 Change from baseline (Visit 1) to day 14 (Visit 2) and day 42 (Visit 4) in Investigator Global Assessment (IGA) (FAS Population)

Table 14.2.2.2 Proportion of treatment successes at Visit 2 and Visit 4 (FAS Population)

Table 14.2.2.3 Change from baseline (Visit 1) to each time point (Visit 2, Visit 3 and Visit 4) in EASI (Eczema Area and Severity Index) score (FAS Population)

Table 14.2.2.4 Change from baseline (Visit 1) to each time point (Visit 2, Visit 3 and Visit 4) in DLQI (Dermatology Life Quality Index) score (FAS Population)

Table 14.2.2.5 Change from baseline (Visit 1) to each time point (Visit 2, Visit 3 and Visit 4) in itching, burning, pain and pruritus, as reported by the subject by VAS (FAS Population)

Table 14.2.2.6 Subject's adherence to treatment (FAS Population)

Table 14.2.2.7 Subject's and Investigator's global evaluation on performance of the study product at the end of the study (Visit 4) by means of a 7-items scale (FAS Population)

Table 14.2.2.8 Subject's overall acceptability of the study product at the end of the study (Visit 4) by means of a 5-item scale (FAS Population)

14.3 Safety data

Table 14.3.1 Analysis of adverse events observed (Safety population)

Table 14.3.2 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: Relife S.r.l.
Protocol ReGl/20/Dec-Der/001

Page 1 of x

Table xx.x.x

(..... Population)

Characteristic	Statistic	DermoRelinema ecofoam
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: xxXXxxxx

14.4.2 Sample table for efficacy analysis – continuous variables

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Protocol ReGI/20/Dec-Der/001

Page 1 of x

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

Endpoint	Statistic	DermoRelisema ecofoam
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

Program: Txxxxxxx xxx.sas CONFIDENTIAL Date: xxXXxxxx

14.4.3 Sample table for efficacy analysis – discrete variables

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Protocol ReGl/20/Dec-Der/001

Page 1 of x

Table xx.x.x.x

(..... Population)

Characteristic	Statistic	DermoRelixema ecofoam
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

Program: Txxxxxxxx xxx.sas

CONFIDENTIAL

Date: xxXXXxxxx

14.4.4 Sample table for adverse events analysis

Sponsor: Relife S.r.l.
Protocol ReGl/20/Dec-Der/001

Page 1 of x

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

AE details	Statistic	DermoRelisema ecofoam
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: xxXXXxxxx

14.4.5 Sample table for adverse events display

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Protocol ReGl/20/Dec-Der/001

Page 1 of x

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

System Organ Class (SOC) . Preferred Term (PT)	DermoRelizema ecofoam 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

The following appendices will be attached to the CIR.:

Appendix 16.1.1 Protocol and Protocol Amendments

Appendix 16.1.2 Sample Case Report Form

Appendix 16.1.3 List of IECs or IRBs - Representative Written Information for Subject and Sample Consent Forms

Appendix 16.1.4 List and Description of Investigators and Other Important Study Participants in the Study Including Curricula Vitae

Appendix 16.1.5 Signature Pages

Appendix 16.1.6 Listing of Subjects Receiving Test Drug/Investigational product from Specific Batches, Where More Than One Batch Was Used

Appendix 16.1.7 Randomization Scheme and Codes

Appendix 16.1.8 Audit Certificates

Appendix 16.1.9 Documentation of Statistical Methods

Appendix 16.1.10 Documentation of Inter-laboratory Standardization Methods and Quality Assurance Procedures, If Used

Appendix 16.1.11 Publications Based on the Study

Appendix 16.1.12 Important Publications Referenced in the Report

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 16.2.1 Discontinued Subjects

Listing 16.2.2 Protocol Deviations

Listing 16.2.3 Subjects Excluded from the Efficacy Analysis

Listing 16.2.4.1 Demographic Data and Disease Details

Listing 16.2.4.2 Medical History

Listing 16.2.4.3 Surgical History

Listing 16.2.4.4 Physical examination

Listing 16.2.5 Compliance

Listing 16.2.6.1 Individual Efficacy Response Data – Investigator Global Assessment (IGA) at each time point (Visit 1, Visit 2, Visit 3 and Visit 4)

Listing 16.2.6.2 Individual Efficacy Response Data – EASI (Eczema Area and Severity Index) score at each time point (Visit 1, Visit 2, Visit 3 and Visit 4)

Listing 16.2.6.3 Individual Efficacy Response Data – DLQI (Dermatology Life Quality Index) score at each time point (Visit 1, Visit 2, Visit 3 and Visit 4)

Listing 16.2.6.4 Individual Efficacy Response Data – Itching, burning, pain and pruritus, as reported by the subject by VAS at each time point (Visit 1, Visit 2, Visit 3 and Visit 4)

Listing 16.2.6.5 Individual Efficacy Response Data – Subject's and Investigator's global evaluation on performance of the study product and Subject's overall acceptability of the study product at the end of the study (Visit 4)

Listing 16.2.7 Adverse Event Listings

Listing 16.2.8 Concomitant Medications

16.2.1 Sample listing

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

Sponsor: Relife S.r.l.
Protocol: ReGl/20/Dec-Der/001

Page 1 of x

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	-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	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	x	x	x.x	-xx.x

Program: Lxxxxxxxx.sas

CONFIDENTIAL

Date: xxXXXxxxx