Final Report

CLINICAL STUDY IN HEALTHY ADULT VOLUNTEERS WITH SENSITIVE SKIN TO VERIFY GOOD SKIN COMPATIBILITY OF THE PRODUCT ARZOLA REF. AR001 LOTE 7409: SINGLE PATCH TEST

RESEARCH CENTER

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ANMAR CLINICAL SERVICES S.L.

PATCH TEST

Code: PT_AKL_20_10

10 August 2020

Sponsor: AKLABS CALIDAD.

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The undersigned, Dr. Domínguez Fernández, certifies that the clinical study with the product **ARZOLA REF. AR001 LOTE 7409** has been performed under my medical responsibility, in accordance with the pertinent experimental protocol and with Good Clinical Practices when applicable.

All the data generated during the study and the results obtained therein have been revised and analyzed and are included in the present Final Clinical Report.

Signed:

Dr. Mª Inmaculada Domínguez Fernández
Dermatologist Medical License 2859198

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1. GENERAL STUDY INFORMATION

The current final report corresponds to the test called “Single Patch Test" (occlusive application of a product to the skin for 48 hours), which allows to verify, in a population of 10 volunteers, good skin compatibility (absence of primary skin irritation) after a single application followed by macroscopic examination performed according to an established numeric scale.

STUDY IDENTIFICATION

TITLE: CLINICAL STUDY IN HEALTHY ADULT VOLUNTEERS WITH SENSITIVE SKIN TO VERIFY GOOD SKIN COMPATIBILITY OF THE PRODUCT ARZOLA REF. AR001 LOTE 7409: SINGLE PATCH TEST

CODE: PT_AKL_20_10

TYPE OF CLINICAL STUDY

Safety test in healthy volunteers with sensitive skin, with two areas of parallel administration, aimed at verifying good skin compatibility of the product **ARZOLA REF. AR001 LOTE 7409**, after a single application, on the skin of the back and under occlusive patch, for 48 hours and a re-assessment at 96 hours.

DESCRIPTION OF THE PRODUCT

PRODUCT: **ARZOLA REF. AR001 LOTE 7409**

COMPOSITION (INCI): Olea europea fruit oil, cera alba, propolis, mel, cannabis xativa L extract, calendula officinalis flower extract, thymus vulgaris extract, lichen extract, lavandula latifolia extract, limonene, linalool.

MANUFACTURER: LADERME, S.L.

RESPONSIBLE FOR PRODUCT SAMPLES

LADERME, S.L.

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COMPANY RESPONSIBLE AND STUDY CENTER FOR STUDY PERFORMANCE

Anmar Clinical Services S.L.
Clínica San Fermín
Avda. Galicia 2A 31003 Pamplona (Navarra)

INVESTIGATORS DATA

Principal Investigator: Dr. Mª Inmaculada Domínguez Fernández
Co-Investigator: Mª Luisa Giráldez Quiroga
Anmar Clinical Services S.L.

STUDY DURATION

The study was performed on the following dates:

EXPERIMENTAL PHASE	from 03 to 07 August 2020.
FINAL REPORT	10 August 2020.

2. OBJECTIVE

The main objective of this study was to verify good skin compatibility of the product **ARZOLA REF. AR001 LOTE 7409**, after a single application, on the skin of the back and under occlusive patch, for 48 hours, in healthy adult volunteers with sensitive skin.

3. SUBJECT SELECTION AND STUDY DEVELOPMENT

Study participants were selected in accordance with the following inclusion and exclusion criteria:

INCLUSION CRITERIA

To be included, the volunteers had to comply with all of the following criteria:

1. Men and women.
2. Aged between 18 and 65 years.
3. 100% sensitive skin.
4. Volunteers with Fitzpatrick skin photo-type I to IV.

5. Adequate cultural level and understanding of the clinical study.
6. To agree to participate voluntarily in the study and grant written Informed Consent.

EXCLUSION CRITERIA

The presence of at least one of the following criteria was the reason of exclusion from the study:

1. Chronic or acute disease at study initiation or in the last 3 weeks prior to inclusion.
2. Skin pathologies in the last 3 weeks prior to study initiation.
3. Receiving pharmacological treatment.
4. Pregnant or breast-feeding women.
5. Subjects with skin spots in the experimental area which could interfere with the evaluation of skin reactions (pigmentation disorders, scars, excessively developed downiness, large amounts of freckles and nevus, sunburns, etc.).
6. Subjects with allergy to any of the study product components.
7. Subjects with allergy to colophony, nickel, aluminum and/or ethanol.
8. Reactivity to adhesive plastic.
9. Intensive sun exposure during the last month prior to study initiation
10. Treatment with acid Vitamin A or its derivates in the last three months prior to study initiation.
11. Treatment with PUVA or UVB in the last month prior to study start.
12. Vaccinated in the last 3 weeks previous to study start.

Ten (10) volunteers were recruited for the study; it is considered that the number of volunteers used in this type of studies is sufficient for the verification of good skin compatibility of a cosmetic product.

All the volunteers followed a series of recommendations indicated by the principal investigator at the study start:

- No cosmetic product or make-up, other than the tested one, should be applied in the experimental area.
- No bath in bathtub, sea or swimming pool nor in sauna or Turkish bath was allowed during the study.
- No vaccination during the study was permitted.
- No sun exposure one week before the study start nor during the study should be undertaken.
- Avoid using too tight clothes
- Avoid intense sports resulting in patch unstick due to excessive sweating.

NOT INCLUDED AND EXCLUDED FROM THE STUDY

A volunteer may abandon the study at any moment, regardless of the reason. These cases are named “not included”.

During the study, the principal investigator may withdraw a volunteer from the study due to non-compliance of the research protocol or due to health reasons. Such cases are named “excluded”.

In case the exclusion of a volunteer is due to negative sensations or discomfort during the study, the principal investigator will collect, in a specific document, the information and follow-up performed from the moment such situation occurs until the physician considers he/she presented total recovery (additional visits could be necessary), as well as conclusions of the case.

The study was performed in the following phases:

SELECTION PHASE

Upon their arrival in the Center, the volunteers were handed over the Participant Information Sheet and once they read and understood it, they granted their written informed consent to be included in the study.

After the signature of the Informed Consent, the volunteers were examined and interviewed and their data, such as personal and demographic data, as well as various aspects related to the skin health, were included in the Participant Clinical History.

Those volunteers who complied with all the inclusion criteria and none of the exclusion criteria were included in the study.

EXPERIMENTAL PHASE

The experimental phase of this study lasted for five days during which each volunteer performed the following visits:

Day 1 (Baseline Visit). The investigator applied the study product, on the skin of the back of the volunteer and covered it with an occlusive patch. Additionally, a second patch was placed, without any product, to discard reactions to the patches themselves.

Day 3 (48-hour evaluation). Upon arrival of the volunteer to the research center, her/his patches were removed. The evaluation of all study parameters was done 30 minutes after the removal of the patches.

Day 5 (96-hour evaluation): Additionally, a re-assessment of the experimental area was performed at 96 hours after application.

The flow chart of the study was as follows:

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	Selection	Day 1	Day 3	Day 5
Clinical history.	+			
Inclusion/exclusion criteria.	+			
Informed Consent.	+			
Application of study product and of product-free patch.		+		
Control.	VS	V1	V2	V3
Removal of the patch and lecture.			+	Re-assessment
Adverse events.			+	+

4. DESCRIPTION OF THE PRODUCT AND EVALUATION ENDPOINTS

STUDY PRODUCT AND ITS APPLICATION

The study product, **ARZOLA REF. AR001 LOTE 7409,** was applied using Finn Chambers Aqua® patch. The total amount of the product was 20 µl in a 50 mm^2 surface and it was applied only once and this patch remained untouched on the skin for 48 hours. At the same time, a second patch was placed, without any product, to rule out any reaction to the patch itself.

After 48 hours, the patches were removed, and the experimental area was evaluated 30 minutes later to discard skin irritation produced by the product. Additionally, a re-assessment was performed at 96 hours after product application to discard delayed signs of irritation.

EVALUATION ENDPOINTS

The main evaluation endpoint was the index of lecture for epicutaneous tests:

Erythema

EVALUATION	SCORE
No erythema.	0
Very slight erythema (hardly visible) in at least ¾ of the application area or visible in a smaller area.	1
Clearly visible erythema, uniformly allocated on at least ¾ of the application area.	2
Important erythema (dark red).	3
Purpuric erythema.	4

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Edema

EVALUATION	SCORE
No edema.	0
Very slight edema and palpable on at least ¾ of the application area, or slight edema on a smaller surface.	1
Slight edema (edges well defined) on at least ¾ of the application area.	2
Severe edema (1 mm thick at less) on a surface greater than the application area.	3
Severe edema (1 mm thick at least) on a surface greater than the application area.	4

Papulae/Vesicles/Bullae/Pustules

EVALUATION	SCORE
No papulae, vesicles, bullae or pustules.	0
Papulae or small vesicles (less than about 1 mm in diameter).	1
Vesicles of 1 to 2 mm of diameter.	2
Pustules.	3
Bullae with clear liquid.	4

Dryness/Desquamation

EVALUATION	SCORE
No dryness and desquamation.	0
Slight dryness = mat, unpolished aspect, on at least ¾ of the application area, or pulverulent (whitish) aspect on a surface smaller than ¾ of the application area.	1
Clear dryness = pulverulent aspect on at least ¾ of the application area, or desquamatory aspect on a surface smaller than ¾ of the application area.	2
Moderate desquamation = desquamatory aspect on at least ¾ of the application area, or presence of thick squamae on a surface smaller than ¾ of the application area.	3
Severe desquamation = presence of thick squamae or at least ¾ of the application area, with possibility of tegument fissuration.	4

Detergent effect

EVALUATION	SCORE
No rugosity.	0
Slight rugosity = slightly worn aspect on at least ¾ of the application area, or clearly worn aspect on a surface smaller than ¾ of the application area.	1
Clear rugosity = clearly worn aspect on at least ¾ of the application area, or very worn aspect (presence of wrinkles with well pronounced crests) on a surface smaller than ¾ of the application area.	2
Moderate rugosity = very worn aspect on at least ¾ of the application area, or presence of deep wrinkles on a surface smaller than ¾ of the application area.	3
Severe rugosity = presence of deep wrinkles on at least ¾ of the application area.	4

Reflectivity

EVALUATION	SCORE
No reflectivity.	0
Slight reflectivity = slightly shiny aspect on at least ¾ of the application area, or clearly shiny aspect on a surface smaller than ¾ of the application area.	1
Clear reflectivity = shiny aspect on at least ¾ of the application area, or varnished aspect on a surface smaller than ¾ of the application area.	2
Moderate reflectivity = glossy aspect on at least ¾ of the application area, or glazed aspect on a surface smaller than ¾ of the application area.	3
Severe reflectivity = glazed aspect, deeply shimmering, on at least ¾ of the application area.	4

Any other abnormality (epidermal erosion, subjective sensations: pruritus, prickling, burning sensation) was also noted.

5. PLANNED ACTIVITIES. COMPLIANCE OF PRE-ESTABLISHED SCHEDULE. SUBJECT FOLLOW-UP.

During the performance of this study, the below schedule was followed:

- Administration of study product: 03 August 2020.
- Removal of patches: 05 August 2020.
- Re-assessment: 07 August 2020.
- Final Report: 10 August 2020.

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PARTICIPANTS FOLLOW-UP

A total of 10 participants were recruited in this study. All of them were included in the study after the signature of the Informed Consent and each volunteer completed it in a correct way.

Participants personal data were considered strictly confidential based on the Organic law 15/1999, of 13 December, on the Protection of Personal Data (BOE 298, 14-12-1999, pages 43088-43099).

ASSESSMENT OF RESPONSE

The main endpoint was the Primary Skin Irritation Index which was evaluated based on the scores described in the chapter “Evaluation Endpoints”.

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6. RESULTS

The following table shows the results obtained after the single application of the product **ARZOLA REF. AR001 LOTE 7409** by healthy adult volunteers with sensitive skin. The determination of the Index of Primary Cutaneous Irritation (P.C.I.) corresponds to the mean of the weighted sum of scoring obtained on the whole panel:

ID	AGE	GENDER	PHOTOTYPE	SKIN TYPE	ERYTHEMA	EDEMA	PAPUL/VESIC/ BULLAE/PUST	DRYNESS/ DESQUAMATION	DETERGENT EFFECT	REFLECTIVITY
1	20	Male	III	Sensitive	0	0	0	0	0	0
2	24	Female	II	Sensitive	0	0	0	0	0	0
3	22	Female	II	Sensitive	0	0	0	0	0	0
4	20	Female	III	Sensitive	0	0	0	0	0	0
5	24	Female	II	Sensitive	0	0	0	0	0	0
6	38	Female	I	Sensitive	0	0	0	0	0	0
7	43	Female	II	Sensitive	0	0	0	0	0	0
8	19	Female	II	Sensitive	0	0	0	0	0	0
9	20	Female	III	Sensitive	0	0	0	0	0	0
10	32	Female	III	Sensitive	0	0	0	0	0	0
Weighting					**1**	**2**	**2**	**0,5**	**0,5**	**0,5**

WEIGHTED TOTAL	0

PRIMARY CUTANEOUS IRRITATION INDEX (P.C.I.	0

= weighted total / number of subjects

Classification (P.C.I)	Weighting (P.C.I.)	Skin compatibility
Non-irritating	<0.25	Very good
Very slightly irritating	=0.25 to <0.5	Good
Slightly irritating	=0.5 to <1	Good
Moderately irritating	=1 to <2	Moderate
Irritating	>= 2	Bad

7. CONCLUSIONS

The conclusion of the clinical study performed with the aim to verify good skin compatibility of the study product **ARZOLA REF. AR001 LOTE 7409** in healthy adult volunteers with sensitive skin, by means of a SINGLE PATCH TEST, was as follows:

- The product **ARZOLA REF. AR001 LOTE 7409** did not produce irritant response in any of the participants.

- The product **ARZOLA REF. AR001 LOTE 7409** resulted **NOT** irritant.

As of the date of the present report and in accordance with the results obtained in the study performed under the adopted experimental conditions, it is concluded that the skin compatibility of the product **ARZOLA REF. AR001 LOTE 7409** is considered as **VERY GOOD.**

It is also confirmed that the product **ARZOLA REF. AR001 LOTE 7409** has been "Tested under dermatological control".

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