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T E S T R E P O R T
18 24 01686

P A T C H T E S T R E P O R T

CHEMISEPT MED

CHEMI-PHARM LTD

SEPTEMBER 2018

Quality Assurance & Control Systems Ltd.,1 Antigonis St., 144 51, Athens, Greece
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48 HOURS PATCH TEST
SKIN TOLERANCE ASSESSMENT
STUDY REPORT

CERTIFICATE ID	:	2018-6449 / 18 24 01686
DISTRIBUTOR	:	N/A
PRODUCT MANUFACTURED BY	:	CHEMI-PHARM AS
RECEIPT DATE	:	07/08/2018
STUDY PERIOD	:	17/09/2018 - 21/09/2018
LAB ID	:	18 24 01686
PRODUCT NAME	:	CHEMISEPT MED
BRAND	:	CHEMI-PHARM
PRODUCT TYPE	:	LEAVE ON, LIQUID
LOT	:	LAB SAMPLE
STUDY SPONSOR	:	QACS Ltd
METHOD	:	48 Hours occlusive patch tests

ASSESSMENT OF SKIN TOLERANCE OF A COSMETIC PRODUCT AFTER A SINGLE APPLICATION DURING 48 HOURS OCCLUSIVE PATCH ON 12 VOLUNTEERS

TABLE OF CONTENTS

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REGULATORY, CONFIDENTIALITY AND ARCHIVING

Regulatory

The study has been conducted by suitably trained, qualified and experienced personnel in accordance with the Declaration of Helsinki (1964) and subsequent revisions (World Medical Association, 1989, Council for International Organizations of Medical Sciences and the World Health Organization, 1993) and taking into consideration the requirements of Directives 2001/20/EC and 2005/28/EC relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use and the COLIPA Guidelines edited on 1997 for the "Product Test Guidelines for the Assessment of Human Skin Compatibility".

Precautions have been taken to avoid the possibility that participants in the study might experience undesirable effects.

Ethical requirements which have been taken into consideration in the planning of the study include:
i) participants are informed volunteers selected after application of inclusion/non inclusion criteria
ii) participants are aware of the purpose and nature of the study and of any foreseeable risks involved in participation in the study and have given written informed consent before the study starts;
iii) a safety evaluation has been conducted on the product tested, before the study starts.
iv) the test procedures conforms to national regulations.
v) the Ethical Review Scientific Committee include medical, non-medical, appropriate experts and lay members; it has consider the general ethics of the test and verified that the safety and integrity of the participants in the test are protected, taking into account information on the ingredient(s);
vi) all reasonable care has been taken to avoid causing excessive skin reactions or other adverse health effects in the participants during the study;
vii) safety procedures are in place in the event of any unexpected/adverse reactions, including appropriate medical cover;
viii) volunteers are rewarded for their time, inconvenience, etc., but the reward is not so great that it would persuade

Confidentiality

Requirements of Law 2472/1997 on the Protection of Individuals with regard to the Processing of Personal Data are taken into consideration. Processing of volunteers personal data is carried out by doctors or other persons rendering medical services, provided that the Controller is bound by medical confidentiality or other obligation of professional secrecy, provided for in Law or code of practice, and data are neither transferred nor disclosed to third parties. Processing is carried out within the laboratory premises and relates to personal data of the volunteers, provided that the latter have given their consent and that such data are neither transferred nor disclosed to third parties. The anonymity of the volunteers is respected within all studies carried out in our laboratories. Each volunteer can be identified by the Investigator, the doctors and all the persons in charge of the study, thanks to his personal volunteer's code.

Archiving

The laboratory book which contains all the information (raw data and results) regarding the study and the study reports are kept in the laboratory archives during 2 years.

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STUDY SUMMARY / ABSTRACT

ASSESSMENT OF SKIN TOLERANCE OF A COSMETIC PRODUCT AFTER A SINGLE APPLICATION DURING 48 HOURS OCCLUSIVE PATCH ON 12 VOLUNTEERS

CERTIFICATE ID	:	2018-6449 / 18 24 01686
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PRODUCT MANUFACTURED BY	:	CHEMI-PHARM AS
RECEIPT DATE	:	07/08/2018
STUDY PERIOD	:	17/09/2018 - 21/09/2018
LAB ID	:	18 24 01686
PRODUCT NAME	:	CHEMISEPT MED
BRAND	:	CHEMI-PHARM
PRODUCT TYPE	:	LEAVE ON, LIQUID
LOT	:	LAB SAMPLE
STUDY SPONSOR	:	QACS Ltd
TEST METHOD	:	Single application - 48 Hours occlusive patch tests
TIME(S) OF ASSESSMENT	:	1 hour after patch removal, then after 24 & 48 hours (72 hours)
PANEL	:	12 healthy adult volunteers
APPLICATION AREA	:	On the back
QUANTITY OF PRODUCT	:	0.02 ml
METHODOLOGY ABSTRACT	:	Treatment sites are assessed before the first application of test material (baseline) and after treatment at 30 minutes after patch removal. Negative controls are used to facilitate evaluation. Skin reactions are scored throughout the test by the same experienced assessor, a dermatologist, who made the baseline assessment and under the same lighting source, following a pre-defined scoring scale. The quantification of the skin irritation is given through a numeric scale (erythema, oedema, dryness/desquamation, vesicles). The average irritant score of the product to be tested is calculated from the average of the quotations obtained for each volunteer, allowing to rank the product from "non irritant to very irritant".
RESULT	:	The average irritant score of the product is 0.00.
CONCLUSION	:	According to the experimental conditions of the study, the test product, can be considered as **Non irritant** regarding Its primary skin tolerance.

The samples will be stored by the laboratory during 1 month from the end test date.
The study report and raw data will be stored by the laboratory during 2 years.

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TYPE AND OBJECTIVE OF THE STUDY

Skin compatibility is defined as the absence of skin irritation under normal conditions of use and reasonably foreseeable misuse, taking into account objective reactions as well as subjective responses such as stinging, burning or itching.
Skin irritation is defined as non-immunological local skin inflammation.

This test involves single application, 48 hour occlusive patch test.
Treatment sites are assessed before the first application of test material (baseline) and after treatment at 30 minutes after patch removal. Negative controls are used to facilitate evaluation. Skin reactions are scored throughout the test by the same experienced assessor, a dermatologist, who made the baseline assessment and under the same lighting source, following a pre-defined scoring scale. The quantification of the skin irritation is given through a numeric scale (erythema, oedema, dryness/desquamation, vesicles). The average irritant score of the product to be tested is calculated from the average of the quotations obtained for each volunteer, allowing to rank the product from "non irritant to very irritant".

The objective of the test is to determine whether or not the product is likely to induce skin irritation under normal

PANEL STUDIED, INCLUSION / NON INCLUSION CRITERIA.

Number of volunteers
A number of 12 volunteers has been recruited to satisfy the objectives of the test.

Panel characteristics
Volunteers are selected on the basis of inclusion and non-inclusion criteria. The volunteers satisfy all the inclusion criteria and are not in conflict with any of the non-inclusion criteria and had a medical examination (health certificate) and a dermatological examination. The volunteers are clearly informed, verbally and in writing, regarding the nature of the study, the timetable, constraints and possible risks. They give their written informed consent before participation in the study.

Inclusion criteria
- ✓ Informed volunteers who agree to follow the conditions specified
- ✓ where appropriate of relevant age : 18-70 years old
- ✓ where appropriate of relevant gender : female and/or male
- ✓ where appropriate of relevant origin and health
- ✓ free from any dermatological problems on the area studied
- ✓ meet the specific study criteria on skin type
- ✓ proof of home address & social security number
- ✓ able to understand the Greek language and the study requirements

Non inclusion criteria
- ✓ volunteers who does not meet the inclusion criteria
- ✓ pregnancy or nursing condition
- ✓ irritated skin on test site(s)
- ✓ blemishes, marks (e.g. tattoos, scars, sunburn) on the test site(s)
- ✓ medication which may affect skin response and/or past medical history
- ✓ presenting skin pathology which may interfere with the aim(s) of the study
- ✓ presenting contact allergy to one of the ingredients of the tested product
- ✓ participation in another simultaneous study
- ✓ participation in a previous study without an appropriate rest period between studies
- ✓ minors or majors protected by the law and people admitted in a sanitary or social institution for other purpose than research

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Study constraints

During the length of the study, the volunteers are asked:

- ✓ Not to put any product, also water on the patches area.
- ✓ Not to have a bath, neither to expose themselves to UV.
- ✓ To avoid all intense sportive activities that could remove the patch.
- ✓ Not to take aspirin, anti-histaminics, corticoids, anti-inflammatories and any other treatment decreasing or avoiding inflammations or allergies or interfering with the skin metabolism.

Volunteers withdrawals

Participants will be withdrawn for the following reasons:

- ✓ they do not follow the conditions of the Study Information Sheet;
- ✓ they suffer any illness or accident or develop any condition during the study which could affect the outcome of the study;
- ✓ they no longer wish to participate in the study.

TEST MATERIAL

CERTIFICATE ID	:	2018-6449 / 18 24 01686
DISTRIBUTOR	:	N/A
PRODUCT MANUFACTURED BY	:	CHEMI-PHARM AS
RECEIPT DATE	:	07/08/2018
STUDY PERIOD	:	17/09/2018 - 21/09/2018
LAB ID	:	18 24 01686
PRODUCT NAME	:	CHEMISEPT MED
BRAND	:	CHEMI-PHARM
PRODUCT TYPE	:	LEAVE ON, LIQUID
LOT	:	LAB SAMPLE
STUDY SPONSOR	:	QACS Ltd
STORAGE CONDITIONS	:	Away from heat and light

A sample of the tested product is kept at the QACS laboratories for 1 month after the end of the study. After this date and unless contrary requirement from the study sponsor, the product will be destroyed.

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METHOD PRINCIPLE

The principle of the study is based on the single application of 0.02ml of tested product, on the skin of the back of adult volunteers. The product is kept in contact with the skin for 48 hours under occlusive patch.

Equipment

The equipment used for the occlusive patch is composed of a small plastic cavity of 0.64 cm^2 with a filter tissue at the bottom which is made to receive the product to test. All this is fixed to a hypoallergenic non woven adhesive tape.

Dose level

The amount of test material applied to each patch 0.02ml is sufficient to fill the chamber and saturate the pad without overflowing from it when applied to the skin.

Test material application

The area on which the patch is applied is previously cleaned up with demineralised water and dried with cellulose cotton wool tissue.
The patches are put on the back of the volunteer.
The products are tested pure or diluted depending on their type and their use.

- ✓ Mostly, the products are tested pure.
- ✓ Rinse-off products are tested diluted at 5%.
- ✓ Detergents are tested diluted at 10%.
- ✓ Hydrophilic products are diluted in demineralised water
- ✓ Lipophilic products are diluted in mineral oil.
- ✓ Powders are put pure in the patch small cavity and then moistened sufficiently with a drop of mineral oil in order to ensure good contact with the skin and avoid the product dispersion while applying the patch.

The patches thus prepared are left in contact 48 hours.

Negative controls

Whilst this activity is always be on a case-by-case basis and will depend on the nature and type of study, the most common approach is to compare the results obtained for the test materials with those of suitable positive and/or negative controls, or with similar materials.
A "negative" control is a patch without any product, applied in the same conditions as the product to be tested:

- ✓ if the product is tested pure: empty patch.
- ✓ if the product is tested diluted: patch with 0.02ml of the solvent used (demineralised water or mineral oil).

Visual assessment

Treatment sites are assessed before the first application of test material (baseline) and after treatment at 30 minutes after patch removal. Negative controls are used to facilitate evaluation.
Skin reactions are scored throughout the test by the same experienced assessor who made the baseline assessment and under the same lighting source, following a pre-defined scoring scale.

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EXAMPLE OF SCORING SCALE

ERYTHEMA

0 = no evidence of erythema

0.5 = minimal or doubtful erythema

1 = slight redness, spotty and diffuse

2 = moderate, uniform redness

3 = strong uniform redness

4 = fiery redness

DRYNESS (SCALING)

0 = no evidence of scaling

0.5 = dry without scaling; appears smooth and taut

1 = fine/mild scaling

2 = moderate scaling

3 = severe scaling with large flakes

OEDEMA

- = absence of oedema

+ = presence of oedema

EXAMPLE OF SCORING SCALE

The results obtained are compared to those obtained on the control zone. The Average Irritation Index (or Primary Skin Irritation) is calculated as the average of readings obtained on the volunteers population.

$$\frac{\left[\sum (\text{marks T48})_{\text{vol 1 to vol n}}\right] / \text{number of readings}}{\text{Number of volunteers}}$$

Classification of the irritant potential

Average irritation index	Classification
0 - 0.08	Non irritant
0.08 - 0.16	Very slightly irritant
0.16 - 0.56	Slightly irritant
0.56 - 1	Moderately irritant
1 - 1.16	Irritant
> 1.16	Very irritant

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RESULTS

Panel description

This study includes 12 healthy adult volunteers whom characteristics are described below.

Volunteers characteristics

VOL ID	VOLUNTEER CODE	SEX	AGE	CHARACTERISTICS	Events occured during the study
1	1129	F	32	Sensitive skin	
2	1288	F	33	Normal skin	
3	1326	F	48	Sensitive skin	
4	1339	F	58	Sensitive skin	
5	1365	F	57	Normal skin	
6	1489	F	35	Sensitive skin	
7	1535	M	44	Normal skin	
8	1752	M	27	Normal skin	
9	1760	F	63	Normal skin	
10	1767	M	67	Normal skin	
11	1925	F	49	Sensitive skin	
12	1937	M	19	Normal skin	

None of the volunteers selected took a treatment contraindicated with the study.

Study withdrawals

No withdrawal of the study happened.

Skin reactions

No skin reaction was noticed by the dermatologist on the reference area for all the volunteers.

Results analysis

Results obtained for each volunteer as well as the corresponding irritation index.

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CERTIFICATE ID : 2018-6449 / 18 24 01686
DISTRIBUTOR : N/A
PRODUCT MANUFACTURED BY : CHEMI-PHARM AS
RECEIPT DATE : 07/08/2018
STUDY PERIOD : 17/09/2018 - 21/09/2018
LAB ID : 18 24 01686
PRODUCT NAME : CHEMISEPT MED
BRAND : CHEMI-PHARM
PRODUCT TYPE : LEAVE ON, LIQUID
LOT : LAB SAMPLE
STUDY SPONSOR : QACS Ltd
STORAGE CONDITIONS : Away from heat and light

VOL ID	VOLUNTEER CODE	SEX	AGE	**ERYTHEMA**	**DRYNESS**	**OEDEMA**	Total readings 48hrs
1	1129	F	32	0	0	0	0
2	1288	F	33	0	0	0	0
3	1326	F	48	0	0	0	0
4	1339	F	58	0	0	0	0
5	1365	F	57	0	0	0	0
6	1489	F	35	0	0	0	0
7	1535	M	44	0	0	0	0
8	1752	M	27	0	0	0	0
9	1760	F	63	0	0	0	0
10	1767	M	67	0	0	0	0
11	1925	F	49	0	0	0	0
12	1937	M	19	0	0	0	0

Total reading 48hrs. all volunteers	**0**
Number of readings	**1**
Total irritation / number of readings	**0**
Irritation index	**0.00**
Result	**Non irritant**

After 48 hours of application, no skin reaction was observed, by the dermatologist on the area treated.
The average irritation index obtained is equal to 0.00.
Readings are performed at 1, 24 and 48 hours after removal of the patches.

The samples will be stored by the laboratory during 1 month from the end test date.
The study report and raw data will be stored by the laboratory during 2 years.

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RESULTS (continued)

DISCUSSION AND CONCLUSION

In the experimental conditions, after a single application of 0.02 ml of the product under occlusive patch and during 48 hours, on 12 healthy adult volunteers and according to the scale used for the interpretation of the results, the CHEMISEPT MED can be considered as Non irritant regarding its primary skin tolerance.

Investigating doctor :

Printed name : Georgios Karras
Date : 21/09/2018

RESULTS AUTHENTICITY

The study concerned by this report was carried out under my responsibility, according to the experimental protocol and the quality plan of the QACS Ltd laboratory, and follows the good clinical practices.
All the observations and data recorded during this trial are reported in this study report.

I certify the rereading of this report and do agree with its content

Study Manager :

Printed name : Dimitrios Tzouvalis
Date : 21/09/2018

This document has been electronically signed by those names that appear on this report and are the authorized signatories.

The samples will be stored by the laboratory during 1 month from the end test date.
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