HUMAN REPEATED INSULT PATCH TEST WITH CHALLENGE

Study report – final version 1.0 of 10/01/2023

STUDY REFERENCES	**EUROFINS EVIC France – OP0000761405MIG** **EUROFINS EVIC Romania – ER 22/217-16**

INVESTIGATIONAL PRODUCT	
Denomination	**F3320**
Reference	**F3320/RD0224E17**
Batch number	**022E017221012H**

SPONSOR	**SODEL** 190 Rue Rene Barthelemy BP 94184-1414 Lisieux Cedex
STUDY MONITOR	**Romain BOISSONNOT**
COORDINATING CENTRE	**EUROFINS EVIC product testing france SAS** 122, rue Croix de Seguey 33000 BORDEAUX – France Tel: +33 5 56 95 59 95 Fax: +33 5 56 95 05 22 *e-mail: evic-blanquefort@evic.fr* **Contact: Dr Clotilde TRARIEUX-FOURAULT** General practitioner
INVESTIGATING CENTRE	**EUROFINS EVIC PRODUCT TESTING ROMANIA S.R.L** 64-66, Marasesti Boulevard, S4 040256 - Bucharest - Romania Tel.: +40 21 335 70 90 Fax: +40 21 335 70 91 *e-mail: evicromania@evic.ro*
GENERAL MANAGER OF THE INVESTIGATING CENTRE	**Dr Chem Eng Elena Alina Nanu** 64-66, Marasesti Avenue 040256 - Bucharest - Romania Tel: +40 21 335 70 90 Fax: +40 21 335 70 91 *e-mail: AlinaNanu@eurofins.com*
MAIN INVESTIGATOR	**Dr Rozalia Olsavszky** (dermatologist) Registered N° (Romanian ministry of health): 461524 (specialist in dermato-venerology doctor, doctor in medical science) Tel: +40 21 335 70 90 Fax: +40 21 335 70 91 *e-mail: RO02_Medical@eurofins.com*
CO-INVESTIGATORS	**Dr. Ioana Miruna Ciurea & Dr. Andra Daiana Duta** (resident dermatologists) Tel: +40 21 335 70 90 Fax: +40 21 335 70 91 *e-mail: RO02_Medical@eurofins.com*

Initiation date of study performance	**07/11/2022**
Completion date of study performance	**17/12/2022**

Date of the study report: 10/01/2023

HUMAN REPEATED INSULT PATCH TEST WITH CHALLENGE

Table of contents

HUMAN REPEATED INSULT PATCH TEST WITH CHALLENGE

English synopsis

STUDY OBJECTIVES	Mainly, to confirm that the application of the investigational product under maximising conditions of exposure in a panel of healthy human adult subjects does not induce delayed contact sensitisation. Secondarily, to assess the skin compatibility of the investigational product during the study.
SPONSOR	**SODEL** 190 Rue Rene Barthelemy BP 94184-1414 Lisieux Cedex
STUDY MONITOR	**Romain BOISSONNOT**
COORDINATING CENTRE	**EUROFINS EVIC product testing france SAS** 122, rue Croix de Seguey 33000 BORDEAUX – France Tel: +33 5 56 95 59 95 Fax: +33 5 56 95 05 22 *e-mail: evic-blanquefort@evic.fr* **Contact: Dr Clotilde TRARIEUX-FOURAULT** General practitioner
INVESTIGATING CENTRE	**EUROFINS EVIC PRODUCT TESTING ROMANIA S.R.L.** 64-66, Marasesti Boulevard, S4 040256 - Bucharest - Romania Tel.: +40 21 335 70 90 Fax: +40 21 335 70 91 *e-mail: evicromania@evic.ro*
GENERAL MANAGER OF THE INVESTIGATING CENTRE	**Dr Chem Eng Elena Alina Nanu** 64-66, Marasesti Avenue 040256 - Bucharest - Romania Tel: +40 21 335 70 90 Fax: +40 21 335 70 91 *e-mail: AlinaNanu@eurofins.com*
MAIN INVESTIGATOR	**Dr Rozalia Olsavszky** (dermatologist) Registered N° (Romanian ministry of health): 461524 (specialist in dermato-venerology doctor, doctor in medical science) Tel: +40 21 335 70 90 Fax: +40 21 335 70 91 *e-mail: RO02_Medical@eurofins.com*
CO-INVESTIGATORS	**Dr. Ioana Miruna Ciurea & Dr. Andra Daiana Duta** (resident dermatologists) Tel: +40 21 335 70 90 Fax: +40 21 335 70 91 *e-mail: RO02_Medical@eurofins.com*
TYPE OF THE STUDY	Monocentric randomised study performed in simple blind, corresponding to the "Test Clinique Final de Sécurité" as defined by the France's Agency for the safety of health products (ANSM). Study project previously approved by a survey committee.
DATES OF STUDY PERFORMANCE	From November 07th to December 17th 2022
INVESTIGATIONAL PRODUCT	**F3320 – Ref. F3320/RD0224E17 – Batch: 022E017221012H**
	Modalities of application in the study: Diluted at 5% with distilled water, under semi-occlusive patch - 160µl

Synopsis (continuation)

STUDY POPULATION	**Number of test subjects: 100** valid cases **Specific inclusion criteria: test subjects** ▪ aged from 18 to 70, ▪ female / male, ▪ with all types of skin on body, ▪ with a phototype (Fitzpatrick): II, III or IV. **Specific non-inclusion criteria: test subjects** • with personal history of adverse reaction to: ethanol, colophony, rubber, nickel, aluminium, patch materials, adhesive plaster • with family or personal history of atopy
METHODOLOGY	**Application of the investigational product**, in healthy human subjects, by a technician, at the investigating centre, to a skin site on the upper back, under maximising conditions of exposure (under semi-occlusive patch) for a defined time Repeated applications 9 times to the same site (induction site) over a period of 3 consecutive weeks, period necessary to induce a possible allergy (induction period) After a minimal 2-weeks rest period, with no product application, single application of the investigational product, under patch, to the induction site and to a virgin site and for a defined time, enabling to reveal a possible induced allergy (challenge phase) **Application in parallel of distilled water** under semi-occlusive patch at the same defined times as the investigational product = control site Skin examination of the application site, before the 1st product application of the induction period and the application of the challenge phase and after each patch removal by the same investigator or technician, supervised by the investigator Reporting of the sensations of discomfort directly by the test subjects to the investigator or technician, during the study Assessment of the allergic potential - checking of the skin compatibility: • Accurate description of the skin reactions observed • Evaluation of the allergic reaction according to the ICDRG scale: ?+, (+), (++), (+++) • Calculation of the percentage of reactive test subjects during the challenge phase and the induction period

English synopsis (continuation)

RESULTS

Characteristics of the included panel

Number of included subjects: 112
Number of exclusions: none
Number of withdrawals (reason): 5 (ref. 19a, 25a, 16c ,22c and 23c) – for personal reasons independent from the study
Number of valid cases: 107

- Age: 21 to 70 (Mean: 58)
- Sex: F/M
- Phototype: II to IV
- Skin types on the application site: with all types of skin on body, including 34% with sensitive skin on body

Checking of the skin compatibility

No reaction was noted on the control site.

For the investigational product:

Induction period			
Type of reaction	**Description of the reaction on the induction site**	**Number and percentage of reactive test subjects**	**Total number and percentage of reactive test subjects**
E: Erythema	None	0 / 0%	0 / 0%
M: Complementary mention	None	0 / 0%	

Challenge phase			
Type of reaction	**Description of the reactions on the induction site and the virgin site**	**Number and percentage of reactive test subjects**	**Total number and percentage of reactive test subjects**
E: Erythema	None	0 / 0%	0 / 0%
M: Complementary mention	None	0 / 0%	
A: ICDRG scale	None	0 / 0%	

OVERALL CONCLUSION

Under the experimental conditions adopted:

- During the induction period, the repeated applications of the product **F3320 – Ref.: F3320/RD0224E17, Batch: 022E017221012H**, diluted at 5% with distilled water, under semi-occlusive patch on a panel of 107 test subjects with all types of skin on body, including 34% with sensitive skin on body, induced no reaction of irritation.

- During the challenge phase, the single application of the investigational product to the induction site and virgin site induced no allergic reaction.

Based on these results, the product has a very good skin compatibility and does not show a sensitizing effect[1].

[1] Absence of sensitizing evidence under experimental conditions adopted can be used as support for specific marketing claim "hypoallergenic". However, the absence of sensitizing evidence do not exclude in absolute manner rarely and accidentally sensitizing episodes on a large population

HUMAN REPEATED INSULT PATCH TEST WITH CHALLENGE

Signatures and dates

Investigator: Dr Rozalia OLSAVSZKY (dermatologist)

I the undersigned, Dr Rozalia Olsavszky, declare that the overall conduct of the study was carried out under my responsibility in accordance with the protocol, the internal procedures and in the spirit of the principles of Good Clinical Practices (International recommendations ICH E6(R2) of 09/11/2016, Directive of the European Parliament and Council 2001/20/EC – OJ/EC of 01/05/2001), Romanian Order No. 904/25.07.2006
I assume the responsibility of the validity of all the raw data obtained during the study which are reported in the present study report.

Date: 11/01/2023

Signature:

General Manager of the investigating center: Dr. Chem. Eng. Elena Alina NANU

I the undersigned, Alina NANU, declare to have designated Rozalia OLSAVSZKY as investigator and ensured that she approved the study protocol with full knowledge of the facts and made it available to the Quality Assurance personnel.

Date: 11/01/2023

Signature:

Person in charge of the quality control: Cristina Borlescu

I the undersigned, Cristina BORLESCU, declare that the reported results accurately and completely reflect the raw data of the study.

Date: 11/01/2023

Signature:

HUMAN REPEATED INSULT PATCH TEST WITH CHALLENGE

I – INITIAL PROTOCOL DESIGN

I.1. STUDY OBJECTIVES

Mainly, this study intended to confirm, in a panel of healthy human adult subjects, that the application of the investigational product, under maximizing conditions of exposure, did not induce delayed contact sensitization.

Secondarily, the skin compatibility of the investigational product was assessed during the study.

I.2. ETHICS

I.2.1. Ethical conduct of the study

The study was performed in accordance with:

- the general principles of medical ethics in clinical research coming from the Declaration of Helsinki (June 1964) and its successive amendments,
- the international recommendations relating to Good Clinical Practices for conducting clinical trials for drugs ICH E6(R2) of 09/11/2016,
- the Directive of the European Parliament and Council 2001/20/EC concerning the harmonization of legislative, statutory and administrative provisions of the member States relating to the application of good clinical practices when conducting clinical trials for drugs for human use – OJ/EC of 01/05/2001,
- the recommendations of Colipa - August 1997: "guidelines for the assessment of human skin compatibility",
- the Romanian Order No. 904/25.07.2006 on approval of rules relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use.

and was in accordance with the REGULATION (EU) 2016/679 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data.

I.2.2. Relevance of the study

On the one hand, the aims of the study were a better knowledge of the skin safety of the investigational product and the confirmation of the absence of allergic potential and the investigational product was not applied under normal conditions of use. So, the test subject had no direct benefit from this study.

On the other hand, the foreseeable risk incurred by the test subjects was a possible allergic reaction to one or several ingredients of the investigational product or a skin irritation due to the finished product applied under maximized conditions (under patch).

Generally in this type of study, the possible adverse effects (as erythema, vesicles…) are limited on the application sites and decrease in some days.

The applications were performed at the investigating centre and supervised by a dermatologist, so the application had to be quickly stopped if necessary, and the clinical follow-up of the reactive test subject(s) had to be done by a competent person.

So, according to the nature and the severity of the possible reaction, the investigator had to define the conduct to be adopted and the suitable steps to ensure the safety of the test subject(s) (for example definitive or temporary exclusion of the test subject(s) concerned from the study, modification of the application conditions of the product…) and had to ensure the clinical follow-up of the test subject(s) concerned, as long as it was necessary.

All the test subjects were included in the study the same day.

So, there was suitability between the aim of the study and its eventual risks and the foreseeable troubles related to the experimental conditions of the protocol.

The skin examination was performed by the investigator or technician, supervised by the investigator, having the appropriate experience.

The experimental conditions of product application created a certain occlusion and favoured the penetration of the ingredients through the skin. If some of them had an allergenic potential, this one was more easily proved by this kind of approach.

The product dose was perfectly controlled and the patch material and the conditions of use of the product were adapted to the product category.

A control site (without investigational product) served as control to take into account the possible effects not directly related to the investigational product but due to the patch material.

The investigational product was tested with other products at the same time, the experimental area chosen (back) enabling to test easily several products (maximum 17 product sites at least 1 cm far apart). The sites of application of the different products and the control site(s) will be chosen according to a clockwise distribution, altering of one rank from a test subject to another, to take into account the variability of the skin reactivity according to the site.

The observance of the experimental conditions by the subjects, who took part in the study, was assessed by a questionnaire at the end of the induction phase and at the end of the challenge.

I.2.3. Survey committee

The study had to be devoid of any foreseeable serious risk for the safety of the test subjects.

So, according to the procedure of the investigating centre, the protocol, the informed consent form and the information concerning the investigational product (particularly referring to its safety) had to be submitted to the opinion of an Institutional Ethics Committee, formed with members belonging to the staff of the investigating centre, but not directly involved in the study.

The Institutional Ethics Committee gave the approval on November 04th 2022.

The study began after the approval of the Institutional Ethics Committee.

I.2.4. Information of the test subject and informed consent form

The information about the study was given to each test subject before the start of the study.

This information was accessible, understandable and suitable for each test subject. It was orally given and then in a written specific document (in Romanian).

This information was completed, if necessary, by the investigator (or the competent person designated by him) who answered all the questions asked by the test subject.

The informed consent form was personal and previous to the start of the study.

It was clear, informed and explicit. It was written and given on the same support as the information on the study, in order to avoid any risk of dispute about its content.

The content of this document particularly specified:

- that the test subject declares to have a health coverage,
- the aim of the study,
- the study design and the experimental conditions of the study,
- the investigational product conditions of use,
- the approximate number of test subjects involved in the study,
- the expected duration of the study (for the test subject),
- the number of visits to the investigating centre, their dates and their duration,
- the study constraints (obligations, restrictions and troubles),
- the reasonable foreseeable risks,
- that skin site photographs can be taken and, in this case, that the test subject will not be recognizable,
- that the test subject will be requested, if necessary, to take part in a complementary test to complete the study,
- the opinion of the of the Institutional Ethics Committee
- the person to contact and the contact telephone number,
- that the personal data of the test subject will be confidentially treated by the study staff, available for the study monitor and possibly consulted (with the authorization of the test subject) by the auditors, the members of the of the Institutional Ethics Committee and the Health Authorities (subject to non-divulgation)
- the ban on taking part simultaneously in other clinical studies that could interfere with the current study,
- the amount of the compensation for the constraints to be undergone,
- the form of compensation in case of possible harm caused by the study (all the costs of health care assumed through the investigating centre),
- the period of exclusion at the end of the study during which the test subject will not be allowed to take part in another clinical study,
- the confidential treatment of the study data,
- that the anonymity of the test subject will be preserved,
- the freedom for the test subject to refuse to participate or to stop his participation at any time without any justification and any legal consequences.

This document was previously approved by the Institutional Ethics Committee.

At the beginning of the study, the inform consent form was dated and signed by the test subject and by the investigator or the competent person designated. The subject received a copy of informed consent form. The signed informed consent form will be kept at the investigating centre.

I.2.5. Confidentiality and identification of the test subject

The information concerning the test subject, required for his recruitment, his inclusion and particularly that related to his health, obtained during the medical examination prior to his admission in the general panel of the investigating centre, formed part of medical secret and was confidentially treated.

The test subject was coded when included in the current study (according to the corresponding procedure of the investigating centre) in order to preserve his anonymity.

If photographs of the skin had to be taken, the test subject had to be non recognizable.

I.2.6. Insurances

Insurance of the investigating centre

The investigating centre and coordinating centre are covered by an insurance guaranteeing its civil responsibility towards the test subjects: HDI-Global SE, Policy no.: 110-01325685-14023 as lead insurer and XL Insurer Company SE as co-insurer: BE00006048LI22A.

Insurance of the coordinating centre
The investigating centre is covered by an insurance guaranteeing its civil responsibility towards the test subjects: HDI Global SE, Policy no.: 01012182-30012.

I.3. INVESTIGATING CENTRE AND STAFF

I.3.1. Investigating centre

The study was performed at Eurofins Evic Romania, certified ISO 9001, ISO 14001 and OHSAS 45001, equipped with material and technical means suitable for clinical researches on cosmetic products and compatible with the safety requirements for human subjects.

I.3.2. Technical staff

The test was performed by a competent investigator and a trained and qualified technical staff.

Main Investigator: Dr Rozalia Olsavszky (dermatologist)

Registered N° (Romanian ministry of health): 461524 (specialist in dermato-venerology doctor, doctor in medical science)
Tel: +40 21 335 70 90
e-mail: ro02_medical@eurofins.com

Co-Investigators: Dr. Ioana Miruna Ciurea & Dr. Andra Daiana Duta (resident dermatologists)
Tel: +40 21 335 70 90
e-mail: ro02_medical@eurofins.com

Technicians in charge of the study: Nicoleta Dumitru & Irina Stancu.
Tel: +40 21 335 70 90

I.3.3. Scientific management

Scientific manager: Dr Chem Eng Elena Alina Nanu
Tel: +40 21 335 70 90
e-mail: AlinaNanu@eurofins.com

I.3.4. Quality assurance staff

Person responsible for quality control: Cristina Borlescu
Tel: +40 21 335 70 90
e-mail: cristinaborlescu@eurofins.com

I.4.COORDINATING CENTRE

The coordinating centre was Eurofins Evic France and the Institute of Dermo-Cosmetic (Idec), department of Eurofins Evic france, certified ISO 9001.

The coordinating centre and the investigating centre are partners and work in the same field of activities; so, the coordinating centre ensured the liaison between the sponsor and the investigating centre and brought to the investigator and the technical staff its own scientific expertise.

I.5. DATES OF STUDY PERFORMANCE

Initiation date of study performance: 07/11/2022

Completion date of study performance: 17/12/2022

I.6. OVERALL STUDY DESIGN

I.6.1. Type of the study

This monocentric clinical study was randomized and performed in simple blind, in a panel of healthy human subjects.

The test subject was used as own control.

I.6.2. General principle of the study

The investigational product had to be applied on **100** test subjects, by a technician, at the investigating centre, under maximized conditions of exposure (under patch) for a defined time. The applications had to be repeated 9 times to the same site (induction site) over a period of 3 consecutive weeks, period necessary to induce a possible allergy (induction phase).

After a minimal 2-week rest period, with no product application, a single application of the investigational product, under patch, to the induction site and to a virgin site and for a defined time, enabling to reveal a possible induced allergy (challenge), had to be performed.

A skin examination of the application site had to be performed before the 1st product application of the induction phase and the application of the challenge and after each patch removal, by the same investigator / technician, supervised by the investigator.

The sensations of discomfort had to be directly reported by the test subjects to the investigator / technician, during the study.

The results of the skin compatibility were descriptively expressed.

Since sensitisation is not a matter of quantification, the possible reactions had to be classified as allergic or not, according to the observation done during the challenge phase compared with the observation done during the induction phase.

I.6.3. Chronology of the study

Induction phase: 3 consecutive weeks			
Operations at the investigating centre	**Experimental times**		
	D1	**D3 - D5 - D8 - D10 - D12 - D15 – D17 - D19**	**D22**
Delivery of the inform consent form Signature of the informed consent form Checking of the inclusion and non-inclusion criteria	●		
Clinical examination of the application site and questioning of the test subject by the investigator or technician supervised by the investigator, before product application	●		
Final inclusion	●		
Application of the investigational product under patch to the defined induction site	●	●	
Removal of the patch at the investigating centre		●	●
Clinical examination of the application site and questioning of the test subject by the investigator or technician supervised by the investigator		●	●
Control of the observance			●

Rest period : 2 consecutive weeks at least (4 weeks at the most)	**No product application**

Challenge phase: 1 week				
Operations at the investigating centre	**Experimental times***			
	D37	**D39**	**D40****	**D41**
Clinical examination of the application site and questioning of the test subject by the investigator or technician supervised by the investigator, before product application	●			
Application of the investigational products under patch to the defined induction site and to a defined virgin site	●			
Removal of the patch at the investigating centre		●		
Clinical examination of the application sites and questioning of the test subject by the investigator or technician supervised by the investigator		●	●	●
Control of the observance			●	●

**Forecasted days*
*** In case of reaction the investigator may consider D40 as a control day*

I.7. STUDY POPULATION

I.7.1. Constitution of the panel of test subjects and mode of recruitment

The investigating centre has at its disposal a general panel of subjects constantly renewed. These subjects come from all social categories. They either volunteer spontaneously arise to the investigating centre or reply to a direct call from the latter. Prior to their admission in this general panel, they are subjected to a medical examination and a detailed medical and cosmetological questionnaire, performed by a general practitioner according to the internal procedure of the investigating centre.

All the data concerning the panel are computerized and on paper.

For the study, the test subjects were selected from this general panel on the basis of inclusion criteria and non-inclusion criteria specific to the study and on their ability to respect the constraints required by the protocol. They were definitely included in the study after a specific questioning and a clinical examination.

I.7.2 . Number of test subjects

The number of test subjects with exploitable data (valid cases[(1)]) at the end of the study had to be at least **100.**

[(1)]valid case = test subject that respected the protocol with no significant deviation which could have some influence on the study results.

The number of test subjects necessary to allow a reliable prediction of the sensitising potential of an investigational product depends on the methods used. The statistical considerations involved in extrapolating from a small test population to a large number of users were discussed in the following publication:

- Henderson C.R., Riley E., Certain statistical considerations in patch testing, J. Invest. Dermatology, 1945, 6, pp. 227-232

It is obvious that studies with numbers of test subjects sufficient to obtain statistically valid data applicable to several thousand consumers are not feasible. Therefore, the value of predictive patch testing does not lie in the precision of the prediction but in screening out the rare sensitising products.

So, referring to the experience acquired in the field of contact allergy to cosmetic products, the number of test subjects, empirically defined in the protocol, was sufficient to confirm, before product launching, the absence of allergenic potential of the investigational product and to achieve the study objectives.

At the beginning of the study, complementary test subjects (+12) had to be included to answer the demand and to compensate the possible withdrawals or exclusions from the study independent of the investigational product.

The test subjects excluded from the study for reasons dependent of the investigational product had to be taken into account in the study results and did not have to be replaced.

If during the study, there was a risk not to have the required number of valid cases (great number of withdrawals…), the sponsor had to be informed and an additional quota of subjects had to be possibly included to reach the target.

At the end of the study, in spite of the precautions taken by the investigating centre, if the number of valid cases was less than the number of test subjects requested by the sponsor, the study monitor had to be informed.

I.7.3. Inclusion criteria

I.7.3.1. General inclusion criteria

According to the protocol, had to be included in the study, the subjects:

- suitable to participate in the study (after the clinical examination and questioning) and corresponding to the quality of "healthy subject" as defined in the corresponding procedure of the investigating centre,
- declaring to have a health coverage,
- signing an "informed consent form" for this study,
- certifying not to take part in another clinical study that could interfere with the current study,
- certifying the truth of the personal information declared to the investigator,
- capable of following directions and reliable to respect the constraints of the protocol (living not too far from the investigating centre, no linguistic and intellectual barrier),
- free to ensure the visits to the investigating centre,
- declaring not to have exposed themselves to a risk of pregnancy for at least 3 months before the beginning of the study and committing themselves to use effective contraceptive method throughout the study (for the women of childbearing potential).

I.7.3.2. Specific inclusion criteria

Subjects:

- aged from 18 to 70,
- female and/or male,
- with all types of skin on body,
- with a phototype (Fitzpatrick): II, III or IV.

I.7.4. Non inclusion criteria

I.7.4.1 General non inclusion criteria

According to the protocol, did not have to be included in the study, the subjects:

- being in exclusion period,
- deprived of freedom by administrative or legal decision or under guardianship,
- who cannot be contacted in case of emergency,
- admitted in a residential care,
- planning a hospitalization during the study,
- belonging to the staff of the investigating centre,
- being of age but protected by law,

- having received vaccination (including the second or third dose of COVID-19 vaccine) within the 2 weeks prior to the study or intending to be vaccinated during the course of the study,
- with personal history of adverse reactions to the same type of product as the investigational product,
- with documented history of contact allergy,
- exhibiting skin marks and/or moles and/or freckles in too great quantity, hyperpilosity on the experimental area able to interfere with the assessment of the possible skin reactions,
- with still visible eczematous reaction, scar or pigmentary after-effects of previous tests on the experimental area,
- under treatment, prior to the study, able to interfere with the interpretation of the study results, particularly:
    - systemic retinoids (isotretinoin per os …) within the 6 months,
    - other systemic anti-acne medication within the 3 months,
    - topical retinoids within the 2 months,
    - other topical anti-acne medication within the month,
    - anti-acne cosmetic products within the 2 weeks (excluding face anti acne products),
    - topical or systemic medication with anti-inflammatory or antihistamine products within the 2 weeks,
    - antibiotics within the 2 weeks,
    - medication for malignancy (of any kind) within the 5 years,
    - desensitisation treatment within the 6 months,
- foreseeing, during the study, a treatment able to interfere with the interpretation of the study results (systemic or topical anti-acne medication, anti-acne cosmetic products, topical or systemic medication with anti-inflammatory or antihistamine, antibiotics, desensitisation treatment, …),
- having had a fever lasting more than 24 hours, within the 8 days prior to the study,
- breastfeeding or pregnant or planning a pregnancy during the study (for the women of childbearing potential),
- having started or changed oestrogen-progesterone contraception or hormonal treatment, within the 3 months prior to the study or foreseeing it for the duration of the study,
- having had any invasive aesthetic cares on chest and back (peeling, laser…) by a dermatologist within the 2 months prior to the study or foreseeing it for the duration of the study,
- having had any non-invasive aesthetic cares on chest and back (scrub, skin cleansing…) by an aesthetician within the month prior to the study or foreseeing it for the duration of the study,
- having received excessive or intensive exposure to sunlight (natural or artificial) within the month prior to the study or foreseeing UV exposures for the duration of the study,
- under treatment with PUVA or UVB within the month prior to the study,
- having participated in a human repeated insult patch test with challenge with or without sun exposure 3 months minimum prior to the study,
- having already participated in 5 clinical studies involving patch test, including 3 human repeated patch tests with or without challenge within the year prior to the study
- foreseeing bath (in bathtub, sea or swimming-pool), sauna or Turkish bath during the study period,
- regularly practicing intensive sport causing sweating and requiring frequent showers.

I.7.4.2. Specific non inclusion criteria

Subjects:

- with family or personal history of atopy
- with personal history of adverse reaction to: ethanol, colophony, rubber, nickel, aluminium, patch materials, adhesive plaster.

I.7.5. Specific information concerning the test subjects and medication

Skin reactivity, history of atopy, contraception (type) and possible current medication will be documented by the investigator / technician, supervised by the investigator or the competent person designated, in the collective case report form (CRF) and mentioned in the study report.

No medication likely to interfere with the study will be allowed during the study; however, if the health state of the subjects justifies some medication (particularly anti-inflammatory drugs), any information relating to this concomitant medication will have to be carefully documented in the case report form and mentioned in the study report.

The investigator will have to exclude the test subjects taking concomitant medication likely to interfere with the study and the interpretation of the results.

I.7.6. Exclusion criteria

According to the study protocol and to the procedures of the investigating centre, had to be excluded from the study, the test subjects:

- who did not comply with the protocol and created deviation resulting in un-exploitable results,
- who took part in another clinical study in another investigating centre,
- who had adverse event (for example: inter-current disease requiring a concomitant medication interfering with the study and the interpretation of the results or severe skin intolerance to the investigational product), incompatible with a good protocol observance.

The temporary or definitive discontinuations decided by the investigator and their dates and reasons had to be carefully documented in the collective case report form (CRF) and mentioned in the study report.

I.7.7. Withdrawal criteria

According to the study protocol and to the procedures of the investigating centre, had to be considered as withdrawals, the test subjects:

- who discontinued the study for personal reasons independent of the study (for example: moving house, new job),
- who did not come to the investigating centre for the checking in spite of phone calling.

The withdrawals and their dates and reasons had to be carefully documented by the investigator in the collective case report form (CRF) mentioned in the study report.

I.7.8. Study constraints imposed on the test subjects

The constraints defined by the procedures of the investigating centre and partly in the study protocol, imposed on the test subjects during the study, were the following ones:

- if justified and asked by the investigator, participation in a complementary test (additional visits to the investigating centre),
- exclusion period at the end of the study (according to the corresponding procedure of the investigating centre and 3 months minimum before starting a human repeated insult patch test with challenge, 1 month minimum before starting another type of study),
- no participation in another clinical study that could interfere with the current study,
- if justified, description of any concomitant medical treatment not excluded by the inclusion and non-inclusion criteria,
- no drug liable to interfere with the study and the interpretation of the results, *e.g.* aspirin (except low dose maintenance therapy), products containing aspirin, antihistamine drugs, anti-inflammatory drugs, antibiotics… (however, if therapeutic requirement: possible exclusion from the study),
- neither initiation of a hormonal treatment nor change of the usual hormonal treatment,
- no change of the mode of contraception,
- no significant change in lifestyle: diet, smoking, sport,…,
- visit to the investigating centre (13/14 times) and respect of the dates and hours of visits,
- neither anti-acne nor anti seborrheic local treatment,
- neither invasive body aesthetic cares (peeling, laser…) nor non-invasive body aesthetic cares (scrub, skin cleansing…) on chest and back, by a dermatologist or an aesthetician in Beauty Salon,
- no application of cosmetic care products to the back,
- no change in usual body hygiene products,
- no introduction of new cosmetic products,
- no intensive sun or UVA exposure (U.V. lamps) during the study and 2 weeks after the end of the study,
- no wearing of too tight or restraining clothes liable to produce frictions on the experimental area and to cause the un-sticking of the patch(es),
- neither Turkish bath nor sauna nor bath (in bathtub or swimming-pool or sea), liable to cause excessive sweating and/or the un-sticking of the patch(es),
- during shower, protection of the experimental area (no violent projection of water, no application of soap, very gentle wiping if necessary) to avoid the un-sticking of the patch(es) or the appearance of inter-current skin irritation,
- no intensive sport liable to cause excessive sweating and the un-sticking of the patch(es),
- no vaccination.

The test subjects were questioned at the end of the induction phase and at the end of the challenge about the respect of the study constraints. These data were documented in the case report form (CRF). The investigator had to assess the importance of the possible deviations in comparison with the experimental conditions required at the beginning of the study and their incidence on the validity of the results.

I.8. INVESTIGATIONAL PRODUCT

I.8.1. Identification of the investigational product

Denomination	F3320
Category	Hygiene
Formula number	F3320/RD0224E17
Batch number	022E017221012H
Galenic form and organoleptic characteristics	Pink gel
Normal foreseeable conditions of use	Wet the hands, remove jewelery and varnish, short nails Put a dose in the hollow of the hands. Rub for 30 sec insisting between the interdigital spaces and the top of the wrists. To rinse carefully and abundantly. Dry with a sigle-use hand towel.

I.8.2. Coding and storage

The sponsor supplied to the investigating centre the investigational product in sufficient quantity for the study and the sampling, in neutral packaging, clearly identified.

Upon receipt, the investigating centre noted the date of product receipt checked the supplied quantities, the investigational product aspect and got sure that the labelling is in accordance with the demand of the sponsor.

If requested, the sponsor received an acknowledgement of receipt, mentioning the remarks of the coordinating centre.

The product units were coded and labelled in Romanian according to the corresponding procedure of the investigating centre.

Number and type of product units	25 plastic flasks with pump 1 plastic flask
Content of product unit	25 x 300 ml 1 x 250 ml
Eurofins Evic Romania code	22-0872

Before starting the study, the storage of the investigational product unit was carried out according to the conditions defined by the sponsor, in the product storage area and a product sample was taken and kept in the sample storage area of the investigating centre for 3 years after the end of the study then destroyed, according to the corresponding procedure of the investigating centre.

Apart from the specific demand of the sponsor, the used and unused product unit will be kept at least 4 weeks after the sending of the final report then destroyed, according to the corresponding procedure of the investigating centre.

I.8.3. Information concerning the investigational product

The investigational product unit had to be supplied with a certificate that particularly referred to:

- the compliance of the ingredients of the investigational product formula with the European Regulation N° 1223/2009 of the European Parliament,
- the safety of the finished investigational products and the absence of foreseeable serious risk for the health of the test subjects.

The qualitative formula of the product had to be supplied to the investigator by the sponsor.

I.8.4. Experimental conditions of application of the investigational product

I.8.4.1. Induction phase

The skin site had to be defined by the technician in charge of the study, on the upper back, on a surface free from scars, moles, freckles and any other skin anomaly, and avoiding the areas of friction with clothes.

The quantity of investigational product had to be measured by the technician in charge of the study with a micropipette (single use tip) and put into the patch.

Before patching, the skin site had to be wiped with a cotton pad and dried, if needed.

The patch containing the investigational product had to be applied, by the technician in charge of the study, on the defined skin site.

According to the protocol, the experimental conditions of patching had to be the following ones:

Patch material	Experimental conditions of use of the investigational product	Quantity to be applied
Semi-occlusive patch: absorbent support in Webril® kept in position by a non woven medical adhesive (surface: 400 mm²)	Diluted at 5% with distilled water	160µl

A semi-occlusive patch, containing 160 µl of distilled water had to be applied in parallel as control to eliminate, when the results were interpreted, the possible inter-current effects due to the adhesive.

The induction consisted of 9 patches applied 3 times a week (for example: Monday, Wednesday and Friday) for a 3 week period.

Patches applied on Mondays and Wednesdays had to be worn for 48 hours ± 4 hours and patches applied on Fridays had to be worn for 72 hours ± 4 hours.

The application was possibly performed on other days of the week, subject to the respect of the three 72-hour contact patches and the six 48-hour contact patches.

Induction phase				
Operations	**Experimental times**			
	D1	**D3 - D5 D10 - D12 D17 - D19**	**D8 - D15**	**D22**
Application of the investigational product under patch to the defined induction site	●	●	●	/
Removal of the patch at the investigating centre	/	● After 48h of contact	● After 72h of contact	● After 72h of contact

The applications had to be repeated on the same site, except in the case of significant irritation/sensitisation reaction.

In case of moderate or severe skin erythema or mild erythema with oedema/infiltration, the sponsor had to be quickly informed and the product application had to be stopped to the induction site defined and continued to a new adjacent site (the change of site being done once only).

In case of suspected allergic reaction the product did not have to be applied again and the case had to be quickly discussed with the coordinating centre and the sponsor. Then, the decision to reapply or not the product had to be jointly taken by the investigator and the sponsor.

During the induction phase, the technician had to precisely locate the test site to be able to retrieve it after the rest period, according to the procedure of the investigating centre.

I.8.4.2. Rest period

No patching had to be performed for a period of 2 weeks minimum (4 weeks maximum) following the end of the induction phase.

The test subjects had to inform the investigator of any reaction occurring during this period.

I.8.4.3. Challenge

The challenge patches had to be applied once after the rest period. The investigational product and the control product had to be applied using the same patching conditions as those used for the induction phase, to 2 sites: a virgin site and the induction site, symmetrically located, if possible. The patches had to be removed 48 hours ± 4 hours after application.

Challenge phase				
Operations	**Experimental times***			
	D37	**D39**	**D40****	**D41**
Application of the investigational product under patch to the defined induction site and to a defined virgin site	●	/	/	/
Removal of the patch at the investigating centre	/	● After 48h of contact	/	/

**Forecasted days*
*** In case of reaction the investigator may consider D39 as a control day*

I.9. CHECKING OF THE SKIN COMPATIBILITY

I.9.1. Recording of the skin reactions

Skin examinations of the application sites had to be performed visually, by the same investigator / technician, supervised by the investigator, under standard "daylight" source:

- during the induction phase:
  - before patching on D1
  - 15 to 30 minutes after patch removal (or more, if redness appeared after the removal of the adhesive) on D3, D5, D8, D10, D12, D15, D17, D19, D22
- during the challenge phase:
  - before patching on D37
  - 15 to 30 minutes after patch removal on D39 (or more, if redness appeared after the removal of the adhesive)
  - 48h +/- 4 hours after patch removal on D41

In case of delayed skin reaction occurring after the 96h grading, the test subject had to contact the investigating centre and the site had to be re-examined by the investigator as long as necessary until reactions disappear.

All adverse reactions had to be followed until resolution.

Concurrently with the clinical examinations performed, the test subjects had to be questioned about the possible sensations of discomfort they felt.

In case of strong sensations of discomfort felt during the patch wearing at home, the test subjects had to inform by phone the investigator. If necessary, the patch was removed and a skin examination was quickly performed by the investigator (before the next planned visit to the investigating centre).

In case of application to a new adjacent site, the original test site had to be scored in parallel with the new test site until completion of the study and the skin scores of this original test site had to be distinctly documented.

Digital photographs of the skin had to be systematically taken when justified (adverse effects).

All the data were recorded in the collective case report form (CRF).

I.9.2. Expression of the results

All the reactions had to be accurately described at each experimental time using the criteria and the scale hereafter.

E = Erythema d= diffuse p = punctuated peri = peripheral	**0** – no visible erythema **0.5** – very slight erythema – barely perceptible **1** – mild erythema – faint pink **2** – moderate erythema – well defined **3** – severe erythema **4** – caustic effect – erosive aspect and/or necrotic aspect

If erythema E ≥ 1 the investigator had to proceed to palpation to assess infiltration/oedema.

M = Complementary mention : Other reactions	
Sv	Soap effect (shiny skin with possibly wrinkles)
D	Desquamation
Dr	Dryness
Hy	Hypopigmentation
C	Skin coloration – hyperpigmentation
Oe	Homogeneous infiltration / oedema
P	Papules
V	Vesicles
Pe	Petechiae
Fr	Follicular reaction
I	Itching at the test site
S	Spreading beyond the patch area (infiltration or erythema)
F	Fissuring
Cr	Exudation and/or Surface encrustation
B	Bullae
Sc	Scab
He	Heating
Pu	Pustules
/	No reaction

The other visible clinical signs had to be described.

M = Complementary mention : Additional comments	
NA	Product not applied
T	Tape reaction
L	Loss of patch during the first 12 hours
N9G	No 9th grading
X	Succeeding patch not applied and succeeding grade (in brackets) denotes a residual reaction
Abs	Test subject absent

For the induction phase and the challenge phase, the results were expressed in percentage of reactive test subjects: for this calculation only the visible signs of reactivity were taken into account: (erythema, oedema, vesicle, bulla, papule…)

I.9.3. Interpretation of the results

I.9.3.1. Allergy

All the test subjects included in the study were taken into account to appreciate the skin allergic potential of the investigational product as long as they were submitted at least to one post application examination at the defined time or else.

The nature, intensity, appearance period from the application, disappearance period from the application, location (induction site and/or virgin site) of the skin reaction and the phase of the study were taken into account for the interpretation of the results.

A = ICDRG scale	
IR	Irritation reaction
-	No allergic reaction
?+	Doubtful reaction (only slight erythema)
(+)	Weak positive reaction (without vesicle): slight erythema and infiltration with presence of small papular elevations, possibly papules
(++)	Strong positive reaction: erythema, papules, vesicles, infiltration
(+++)	Extreme positive reaction: intense erythema, oedema, coalescent vesicles (bullae)

A site where erythema was graded 2 or more during the challenge (with or without infiltration) had to be evaluated on subsequent days to note whether the reaction diminished or increased, in order to differentiate between an allergic or an irritant reaction. A rapidly diminishing reaction could be indicative of irritation. A reaction with infiltration / oedema that persisted or increased over time usually could indicate an allergic reaction.

If the possible allergic reaction was observed during the induction phase, it could be the revelation of an allergy previously contracted or the revelation of an allergy precociously induced by the investigational product.

If the possible allergic reaction was observed during the challenge phase (similar responses observed on the virgin site and on the induction site), it could be the revelation of an allergy induced during the induction phase by the investigational product.

In case of suspected allergic reaction, the sponsor had to be quickly informed.
In order to confirm the possible allergic reaction, an additional application (rechallenge) had to be proposed to the test subject with the agreement of the sponsor, at least 3 weeks after complete disappearance of the reaction. The experimental conditions of this complementary test had to be jointly defined case by case by the investigator and the study monitor.

I.9.3.2. Irritation

All the test subjects included in the study were taken into account to appreciate the skin irritant potential of the investigational product as long as they were submitted at least to one post application examination at the defined time or any other time.

To appreciate the skin irritant potential, the interpretation of the results was based on the experience of the investigator in this field. The skin compatibility of the investigational product was classified as: very good, good, moderate or bad, in the study conditions.

If justified in case of reactivity in some test subjects, a complementary study had to be possibly carried out in these test subjects, after agreement of the sponsor. The experimental conditions of this study had to be defined by the investigator, case by case.

I.10. SUSPENSION OF THE STUDY

The investigator had to stop the study if it showed a risk for the health or the integrity of the test subjects.

The date of the suspension and the reasons had to be carefully documented by the investigator in the case report form.

The study monitor had to be informed promptly by phone, fax or e-mail by the coordinating centre.

The sponsor was able to stop the study at any time for administrative reasons or other ones.

I.11. ADVERSE EVENTS

I.11.1. Definitions

Any topical product can induce, when used in Human, according to individual sensitivities, a local and minor reactivity, defined as follows: any slight local reaction of intolerance or sensation of discomfort, occurring in a test subject during a clinical study, completely reversible, expected, due to the investigational product and which does not question the observance of the study protocol or the good implementation of the study.

The following definitions will be used:

- **adverse event**: any harmful event with or without relationship with the investigational product, occurring in a test subject during a clinical study.
- **suspicion of adverse effect**: any adverse event with a quite possible relationship with the investigational product.
- **adverse effect**: any harmful and unwanted reaction, due to the investigational product, occurring in a test subject during a clinical study.
- **unexpected adverse effect**: any adverse effect due to the investigational product, the nature, the intensity and/or the evolution of which do not agree with the product information.
- **serious adverse event / effect**: any adverse event or adverse effect that causes death, endangers test subject's life, induces an hospitalisation or the prolongation of the hospitalisation, causes severe and lasting incapacity or handicap or induces congenital anomaly or malformation.

I.11.2. Data collection

The investigator had to accurately describe the adverse event and had to appreciate its seriousness. According to the corresponding procedure of the investigating centre, he had to define the link of causality between this event and the investigational product, on the basis of the symptoms, the chronology, the results of the possible specific complementary tests undertaken and any available information.

The imputability of the product had to be assessed according to the scale: very likely, likely, possible, questionable, excluded.

I.11.3. Conduct to be adopted in case of adverse event

Faced with an adverse event, the investigator had to freely define, case by case, the conduct to be adopted and the suitable steps to ensure the safety of the test subject concerned and of the other test subjects included in the study.

In case of suspicion of adverse effect (with a quite possible relationship with the investigational product), the investigator had to ensure the clinical follow-up of the test subject concerned, as long as necessary.

I.11.4. Communication with the study monitor

According to the corresponding procedure of the coordinating centre, the serious adverse events and the adverse effects had be notified as soon as possible and within 24 hours at the latest, by the coordinating centre to the study monitor, by phone, fax or e-mail.

The investigator had to send an adverse event form to the study monitor and to the coordinating centre.

If justified, the investigator had to give to the coordinating centre and to the study monitor complementary information when available.

I.12. RAW DATA RECORDING AND STUDY REPORT FILING

All the data gathered during the study were recorded accurately, legibly and indelibly by the investigator or the technician in charge of the study, under his control, in the collective case report form.

Each page of this document was initialled by the technician; the whole was verified and validated by the investigator.

The content of this study report took into account the recommendations of the Colipa related to the assessment of the efficacy of cosmetic products (May 2008) and the explanatory note related to the structure and the content of the reports of clinical studies – ICH E3, of 28/11/1995.

At the end of the study, the information concerning the investigational product, the information concerning the test subjects (collective CRF, informed consent forms) were filed and will be kept for 10 years, in the filing area of the investigating centre and the information related to the conduct of the study (protocol signed by the sponsor, copy of this study report….) were filed and will be kept for 10 years, in the filing area of the investigating centre.

At the end of this period, the sponsor will choose among the 3 options:

- return of the study documentation to the sponsor,
- filing of the study documentation in the filing area of the investigating and/or coordinating centre, based on a specific contract,
- destruction of the study documentation (after sponsor's written and signed authorization).

I.13. REFERENCE

The methodology used was an adaptation from that described by Marzulli and Maibach (Human Repeated Insult Patch Test for delayed contact hypersensitivity: HRIPT)

- Marzulli F.N., Maibach H.I., Contact allergy: predictive testing in man, Contact Dermatitis, 1976, 2, pp. 1-17

- V.T. Politano, A.M. Api / Regulatory Toxicology and Pharmacology 52 (2008) 35–38

II – PRACTICAL CONDITIONS OF STUDY PERFORMANCE

II.1. PROTOCOL ADHERENCE

II.1.1. Study population

II.1.1.1. Number of test subjects

Number of test subjects included in the study	**112**	
Withdrawals	**Test subjects concerned**	**Date and reasons**
	Ref. 19a	16/11/2022 - for personal reasons independent from the study
	Ref. 25a	11/11/2022 - for personal reasons independent from the study
	Ref. 16c	16/11/2022 - for personal reasons independent from the study
	Ref. 22c	14/11/2022 - for personal reasons independent from the study
	Ref. 23c	14/11/2022 - for personal reasons independent from the study
Exclusion	**Test subjects concerned**	**Date and reasons**
	None	Not applicable
Adverse events	**Test subjects concerned**	**Date and reasons**
	None	Not applicable
Valid cases	**107**	

The number of recruited test subjects took into account the inclusion criteria, the constraints of the study and the period of the study performance.

At the beginning of the study, complementary test subjects (+12) were included to compensate the possible withdrawals or exclusions from the study independent of the investigational product.

II.1.1.2. Inclusion and non inclusion criteria

All the test subjects corresponded to the inclusion and non inclusion criteria.

The individual typological characteristics of the test subjects are reported in **Appendix 1**, and recapitulated below for the whole panel:

Age (years old)	**Included test subjects**	**Valid cases**
Minimum	21	21
Maximum	70	70
Mean	58	58
Median	62	61

Criteria	Included test subjects		Valid cases	
	Nb	%	Nb	%
Phototype				
II	33	29%	31	29%
III	74	66%	71	66%
IV	5	4%	5	5%
Sex				
Male	19	17%	18	17%
Female	93	83%	89	83%

II.1.1.3. Specific information concerning the test subjects

The answers of the test subjects concerning the skin reactivity, the history of atopy, contraception (type) and the current medication are reported in **Appendix 2.**

II.1.1.4. Study constraints imposed on the test subjects

All the constraints of the study, defined in the protocol, were respected by the test subjects who completed the study.

II.1.2 . Investigational product

Experimental conditions of application of the investigational product

All the experimental conditions of application at the investigating centre were respected, as defined in the protocol, except for the challenge phase which was performed on D37, D39, D41 instead of D36, D38 and D40, due to administrative reasons. Also, there were 18 products tested instead of maximum 17 on 18 subjects from panel ER 22/217a.

The investigator judged this deviation with no incidence on the interpretation of the results.

II.1.3. Checking of the skin compatibility: recording of the skin reactions

All the skin examinations and questioning of the test subjects were performed in accordance with the conditions defined in the protocol.

III – RESULTS

III.1. RESULTS / DISCUSSION

III.1.1. Checking of the skin compatibility

For the investigational product, the individual data of the skin examination and questioning of the test subjects are reported in **Appendix 3**.

Induction phase			
Type of reaction	**Description of the reaction on the induction site**	**Number and percentage of reactive test subjects**	**Total number and percentage of reactive test subjects**
E: Erythema	None	0 / 0%	0 / 0%
M: Complementary mention	None	0 / 0%	

Challenge			
Type of reaction	**Description of the reactions on the induction site and the virgin site**	**Number and percentage of reactive test subjects**	**Total number and percentage of reactive test subjects**
E: Erythema	None	0 / 0%	0 / 0%
M: Complementary mention	None	0 / 0%	
A: ICDRG scale	None	0 / 0%	

For the control product, the individual data of the skin examination and questioning of the test subjects are reported in **Appendix 4.**

Induction phase			
Type of reaction	**Description of the reaction on the induction site**	**Number and percentage of reactive test subjects**	**Total number and percentage of reactive test subjects**
E: Erythema	None	0 / 0%	0 / 0%
M: Complementary mention	None	0 / 0%	

Challenge			
Type of reaction	**Description of the reactions on the induction site and the virgin site**	**Number and percentage of reactive test subjects**	**Total number and percentage of reactive test subjects**
E: Erythema	None	0 / 0%	0 / 0%
M: Complementary mention	None	0 / 0%	
A: ICDRG scale	None	0 / 0%	

III.2. OVERALL CONCLUSION

Under the experimental conditions adopted:

- During the induction period, the repeated applications of the product **F3320 – Ref. F3320/RD0224E17 – Batch: 022E017221012H, diluted at 5% with distilled water,** under semi-occlusive patch on a panel of 107 test subjects with all types of skin on body, including 34% with sensitive skin on body, induced no reaction of irritation.

- During the challenge phase, the single application of the investigational product to the induction site and virgin site induced no allergic reaction.

Based on these results, the product has a very good skin compatibility and does not show a sensitizing effect[2].

III.3. QUALITY CONTROL AND QUALITY ASSURANCE

The study was performed in compliance with the procedures of the investigating centre, established according to the regulations in force.

The investigator, in charge of the performance of the study, made sure of the quality of the work of the technical staff, particularly concerning the respect of the protocol and its appendices, the collection of raw data, the management of the investigational product.

The personnel of the Quality Assurance department controlled that the study documentation was present, dated and signed.

The personnel of the Quality Assurance department regularly controls that the protocol and working procedures relevant to this type of study are duly applied.

[2] Absence of sensitizing evidence under experimental conditions adopted can be used as support for specific marketing claim "hypoallergenic". However, the absence of sensitizing evidence does not exclude in absolute manner rarely and accidentally sensitizing episodes on a large population.

APPENDICES

Appendix 1/1

TYPOLOGICAL CHARACTERISTICS OF THE TEST SUBJECTS

Test subjects Ref.	**age** *(years)*	**sex** *F=female M=male*	**phototype**[1]
1a	43	F	II
2a	34	F	III
3a	44	F	III
4a	51	F	III
5a	40	F	III
6a	55	F	II
7a	52	F	III
8a	57	F	III
9a	43	F	II
10a	59	F	III
11a	69	M	III
12a	35	M	II
13a	69	F	II
14a	55	F	III
15a	51	F	III
16a	68	F	II
17a	70	F	II
18a	55	M	III
19a	55	F	II
20a	31	F	III

Legends: *Withdrawal*

[1] ***phototype: Type I****: Always burns easily, never tans,* ***Type II****: Always burns easily, tans minimally,* ***Type III****: Burns moderately, tans gradually,* ***Type IV****: Burns slightly, always tans easily,* ***Type V****: Burns rarely, tans intensely,* ***Type VI****: Never burns, strongly pigmented*

Appendix 1/2

TYPOLOGICAL CHARACTERISTICS OF THE TEST SUBJECTS

Test subjects Ref.	**age** *(years)*	**sex** *F=female M=male*	**phototype**[1]
21a	58	F	III
22a	54	F	III
23a	50	M	III
24a	39	M	III
25a	41	F	III
26a	69	F	III
27a	59	F	III
28a	53	F	III
29a	55	F	III
30a	47	F	III
31a	58	F	III
32a	51	F	III
33a	58	M	III
34a	59	F	III
35a	50	F	III
36a	54	F	III
37a	41	F	II
38a	46	F	III
39a	40	F	III
40a	49	M	III
41a	53	F	III
42a	54	F	II

Legends: *Withdrawal*

[1] ***phototype: Type I****: Always burns easily, never tans,* ***Type II****: Always burns easily, tans minimally,* ***Type III****: Burns moderately, tans gradually,* ***Type IV****: Burns slightly, always tans easily,* ***Type V****: Burns rarely, tans intensely,* ***Type VI****: Never burns, strongly pigmented*

Appendix 1/3

TYPOLOGICAL CHARACTERISTICS OF THE TEST SUBJECTS

Test subjects Ref.	**age** *(years)*	**sex** *F=female M=male*	**phototype**[1]
43a	50	F	II
44a	23	M	III
45a	59	F	II
46a	53	F	II
47a	37	M	III
48a	41	F	II
49a	46	F	III
50a	54	M	III
51a	52	M	II
52a	21	F	II
53a	54	F	III
54a	54	F	II
55a	58	F	III
56a	55	F	III
1c	62	F	II
2c	60	F	II
3c	66	F	II
4c	65	F	III
5c	61	F	III
6c	66	F	IV
7c	63	F	II
8c	68	M	III
9c	62	F	IV

Legends:

*[1]**phototype: Type I**: Always burns easily, never tans, **Type II**: Always burns easily, tans minimally, **Type III**: Burns moderately, tans gradually, **Type IV**: Burns slightly, always tans easily, **Type V**: Burns rarely, tans intensely, **Type VI**: Never burns, strongly pigmented*

Appendix 1/4

TYPOLOGICAL CHARACTERISTICS OF THE TEST SUBJECTS

Test subjects Ref.	**age** *(years)*	**sex** *F=female M=male*	**phototype**[1]
10c	64	F	III
11c	62	F	III
12c	38	F	III
13c	61	F	III
14c	64	F	IV
15c	62	F	III
16c	69	F	II
17c	68	F	III
18c	67	F	III
19c	69	F	IV
20c	66	M	II
21c	70	F	III
22c	62	F	III
23c	64	M	III
24c	65	F	II
25c	63	F	III
26c	67	M	III
27c	69	F	III
28c	60	F	III
29c	69	F	III
30c	64	F	II
31c	69	F	II
32c	67	F	II
33c	70	F	III

Legends: *Withdrawal*

[1]***phototype: Type I****: Always burns easily, never tans,* ***Type II****: Always burns easily, tans minimally,* ***Type III****: Burns moderately, tans gradually,* ***Type IV****: Burns slightly, always tans easily,* ***Type V****: Burns rarely, tans intensely,* ***Type VI****: Never burns, strongly pigmented*

Appendix 1/5

TYPOLOGICAL CHARACTERISTICS OF THE TEST SUBJECTS

Test subjects Ref.	**age** *(years)*	**sex** *F=female M=male*	**phototype**[1]
34c	68	F	II
35c	67	F	III
36c	63	F	III
37c	67	F	III
38c	68	M	II
39c	69	F	III
40c	65	F	II
41c	66	F	III
42c	62	F	III
43c	69	F	II
44c	65	F	III
45c	65	M	IV
46c	65	F	III
47c	66	F	III
48c	62	M	III
49c	67	F	III
50c	63	F	II
51c	65	F	III
52c	66	F	III
53c	63	F	III
54c	67	F	II
55c	64	M	III
56c	63	F	III

Legends:

*[1] **phototype: Type I**: Always burns easily, never tans, **Type II**: Always burns easily, tans minimally, **Type III**: Burns moderately, tans gradually, **Type IV**: Burns slightly, always tans easily, **Type V**: Burns rarely, tans intensely, **Type VI**: Never burns, strongly pigmented*

Appendix 2/1

SPECIFIC INFORMATION CONCERNING THE TEST SUBJECTS

Test subjects Ref.	Sensitive (declarative) / reactive skin on body	Atopy	Current medication except for contraceptive pills	Contraception
			If yes *(specify commercial denomination, active substance and dosage, pathology treated)*	**If Yes** *(Type to be specified)*
1a	x	/	/	CONDOM
2a	x	/	/	CONDOM
3a	x	/	/	CONDOM
4a	/	/	/	CONDOM
5a	/	/	/	CONDOM
6a	/	/	/	NC (MENOPAUSE)
7a	/	/	/	NC (MENOPAUSE)
8a	/	/	/	NC (MENOPAUSE)
9a	x	/	/	CONDOM
10a	/	/	/	NC (MENOPAUSE)
11a	x	/	/	NC (MALE)
12a	/	/	/	NC (MALE)
13a	x	/	/	NC (MENOPAUSE)
14a	/	/	/	NC (MENOPAUSE)
15a	x	/	/	NC (MENOPAUSE)
16a	/	/	/	NC (MENOPAUSE)
17a	/	/	/	NC (MENOPAUSE)
18a	/	/	/	NC (MALE)
19a	/	/	/	CONDOM
20a	/	/	/	CONDOM

Legends: / = no *Withdrawal* *NC: Not Concerned*

Appendix 2/2

SPECIFIC INFORMATION CONCERNING THE TEST SUBJECTS

Test subjects Ref.	Sensitive (declarative) / reactive skin on body	Atopy	Current medication except for contraceptive pills	Contraception
			If yes *(specify commercial denomination, active substance and dosage, pathology treated)*	**If Yes** *(Type to be specified)*
21a	x	/	/	NC (MENOPAUSE)
22a	/	/	/	NC (MENOPAUSE)
23a	/	/	/	NC (MALE)
24a	x	/	/	NC (MALE)
25a	x	/	/	CONDOM
26a	/	/	/	NC (MENOPAUSE)
27a	x	/	/	NC (MENOPAUSE)
28a	/	/	/	NC (MENOPAUSE)
29a	/	/	/	NC (MENOPAUSE)
30a	/	/	/	CONDOM
31a	/	/	/	NC (MENOPAUSE)
32a	/	/	/	CONDOM
33a	/	/	/	NC (MALE)
34a	x	/	/	NC (MENOPAUSE)
35a	/	/	/	CONDOM
36a	/	/	/	NC (MENOPAUSE)
37a	x	/	/	CONDOM
38a	/	/	/	CONDOM
39a	/	/	/	CONDOM
40a	/	/	/	NC (MALE)

Legends: / = no *Withdrawal* *NC: Not Concerned*

Appendix 2/3

SPECIFIC INFORMATION CONCERNING THE TEST SUBJECTS

Test subjects Ref.	Sensitive (declarative) / reactive skin on body	Atopy	Current medication except for contraceptive pills	Contraception
			If yes *(specify commercial denomination, active substance and dosage, pathology treated)*	**If Yes** *(Type to be specified)*
41a	/	/	/	NC (MENOPAUSE)
42a	x	/	/	NC (MENOPAUSE)
43a	/	/	/	CONDOM
44a	/	/	/	NC (MALE)
45a	x	/	/	NC (MENOPAUSE)
46a	/	/	/	NC (MENOPAUSE)
47a	x	/	/	NC (MALE)
48a	/	/	/	CONDOM
49a	x	/	/	CONDOM
50a	/	/	/	NC (MALE)
51a	x	/	/	NC (MALE)
52a	/	/	/	CONDOM
53a	/	/	/	NC (MENOPAUSE)
54a	/	/	/	NC (MENOPAUSE)
55a	/	/	/	NC (MENOPAUSE)
56a	/	/	/	NC (MENOPAUSE)
1c	x	/	/	NC (MENOPAUSE)
2c	x	/	/	NC (MENOPAUSE)
3c	x	/	/	NC (MENOPAUSE)
4c	/	/	/	NC (MENOPAUSE)
5c	/	/	/	NC (MENOPAUSE)
6c	/	/	/	NC (MENOPAUSE)
7c	/	/	/	NC (MENOPAUSE)
8c	/	/	/	NC (MALE)

Legends: / = no *NC: Not Concerned*

Appendix 2/4

SPECIFIC INFORMATION CONCERNING THE TEST SUBJECTS

Test subjects Ref.	Sensitive (declarative) / reactive skin on body	Atopy	Current medication except for contraceptive pills	Contraception
			If yes *(specify commercial denomination, active substance and dosage, pathology treated)*	**If Yes** *(Type to be specified)*
9c	/	/	/	NC (MENOPAUSE)
10c	x	/	/	NC (MENOPAUSE)
11c	x	/	/	NC (MENOPAUSE)
12c	/	/	/	CONDOM
13c	x	/	/	NC (MENOPAUSE)
14c	x	/	/	NC (MENOPAUSE)
15c	/	/	/	NC (MENOPAUSE)
16c	x	/	/	NC (MENOPAUSE)
17c	/	/	/	NC (MENOPAUSE)
18c	/	/	/	NC (MENOPAUSE)
19c	/	/	/	NC (MENOPAUSE)
20c	/	/	/	NC (MALE)
21c	/	/	/	NC (MENOPAUSE)
22c	/	/	/	NC (MENOPAUSE)
23c	/	/	/	NC (MALE)
24c	/	/	/	NC (MENOPAUSE)
25c	x	/	/	NC (MENOPAUSE)
26c	/	/	/	NC (MALE)
27c	/	/	/	NC (MENOPAUSE)
28c	x	/	/	NC (MENOPAUSE)
29c	x	/	/	NC (MENOPAUSE)
30c	x	/	/	NC (MENOPAUSE)
31c	x	/	/	NC (MENOPAUSE)
32c	x	/	/	NC (MENOPAUSE)

Legends: / = no *Withdrawal* *NC: Not Concerned*

Appendix 2/5

SPECIFIC INFORMATION CONCERNING THE TEST SUBJECTS

Test subjects Ref.	Sensitive (declarative) / reactive skin on body	Atopy	Current medication except for contraceptive pills	Contraception
			If yes *(specify commercial denomination, active substance and dosage, pathology treated)*	**If Yes** *(Type to be specified)*
33c	/	/	/	NC (MENOPAUSE)
34c	/	/	/	NC (MENOPAUSE)
35c	/	/	/	NC (MENOPAUSE)
36c	/	/	/	NC (MENOPAUSE)
37c	/	/	/	NC (MENOPAUSE)
38c	x	/	/	NC (MALE)
39c	/	/	/	NC (MENOPAUSE)
40c	/	/	/	NC (MENOPAUSE)
41c	/	/	/	NC (MENOPAUSE)
42c	x	/	/	NC (MENOPAUSE)
43c	x	/	/	NC (MENOPAUSE)
44c	x	/	/	NC (MENOPAUSE)
45c	/	/	/	NC (MALE)
46c	/	/	/	NC (MENOPAUSE)
47c	/	/	/	NC (MENOPAUSE)
48c	/	/	/	NC (MALE)
49c	/	/	/	NC (MENOPAUSE)
50c	/	/	/	NC (MENOPAUSE)
51c	/	/	/	NC (MENOPAUSE)
52c	/	/	/	NC (MENOPAUSE)
53c	/	/	/	NC (MENOPAUSE)
54c	/	/	/	NC (MENOPAUSE)
55c	/	/	/	NC (MALE)
56c	/	/	/	NC (MENOPAUSE)

Legends: / = no *NC: Not Concerned*

Appendix 3-1/1

INVESTIGATIONAL PRODUCT: F3320 – Ref. F3320/RD0224E17 – Batch: 022E017221012H
SKIN EXAMINATION AND QUESTIONING DURING THE INDUCTION PHASE

***E: Erythema**: **0** = no visible erythema, **0.5** = very slight erythema – barely perceptible, **1** = mild erythema – faint pink, **2** = moderate erythema – well defined, **3** = severe erythema, **4** = caustic effect – erosive aspect and/or necrotic aspect*
d= diffuse / p = punctuated / peri = peripheral

***M: Additional comments/Others reactions: H or Oe** = Homogeneous infiltration / oedema, **P** = Papules, **V** = Vesicles, **B** = Bullae, **Pe** = Petechiae, **S:** Spreading beyond the patch, **SV** = Soap effect (shiny skin with possibly wrinkles), **F** = Fissuring , **D** = Desquamation, **Dr** = Dryness, **C** = Skin coloration, hyperpigmentation, **HY** = Hypopigmentation, **Fr** = Follicular reaction, **NA** = Product not applied, **T**= Tape reaction, **I** = Itching at the test site, **Cr** = Exsudation and/or Surface encrustation, **Sc** = Scab, **Pr** = Pruritus, **He** = Heating, **Pu** = Pustules, * = Additional free comments, **N9G** = No 9th grade, **Abs or "–"** = Subject absent, **MU** = Make-up patch*

/: no reaction

Test subjects reference	Type of reaction	Experimental times									
		D1	D3	D5	D8	D10	D12	D15	D17	D19	D22
1a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
2a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
3a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
4a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
5a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
6a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
7a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
8a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
9a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
10a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
11a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
12a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
13a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
14a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
15a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
16a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
17a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
18a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
19a	E	0	0	0	0						
	M	/	/	/	/						
20a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/

Legends: *Withdrawal*

Appendix 3-1/2

INVESTIGATIONAL PRODUCT: F3320 – Ref. F3320/RD0224E17 – Batch: 022E017221012H
SKIN EXAMINATION AND QUESTIONING DURING THE INDUCTION PHASE

Test subjects reference	Type of reaction	Experimental times									
		D1	D3	D5	D8	D10	D12	D15	D17	D19	D22
21a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
22a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
23a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
24a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
25a	E	0	0								
	M	/	/								
26a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
27a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
28a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
29a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
30a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
31a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
32a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
33a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
34a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
35a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
36a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
37a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
38a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
39a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
40a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
41a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
42a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
43a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
44a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/

Legends: *Withdrawal*

Appendix 3-1/3

INVESTIGATIONAL PRODUCT: F3320 – Ref. F3320/RD0224E17 – Batch: 022E017221012H
SKIN EXAMINATION AND QUESTIONING DURING THE INDUCTION PHASE

Test subjects reference	Type of reaction	Experimental times									
		D1	D3	D5	D8	D10	D12	D15	D17	D19	D22
45a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
46a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
47a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
48a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
49a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
50a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
51a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
52a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
53a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
54a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
55a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
56a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
1c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
2c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
3c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
4c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
5c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
6c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
7c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
8c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
9c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
10c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
11c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
12c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
13c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
14c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
15c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/

Appendix 3-1/4

INVESTIGATIONAL PRODUCT: F3320 – Ref. F3320/RD0224E17 – Batch: 022E017221012H
SKIN EXAMINATION AND QUESTIONING DURING THE INDUCTION PHASE

Test subjects reference	Type of reaction	Experimental times									
		D1	D3	D5	D8	D10	D12	D15	D17	D19	D22
16c	E	0	0	0	0						
	M	/	/	/	/						
17c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
18c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
19c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
20c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
21c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
22c	E	0	0	0							
	M	/	/	/							
23c	E	0	0	0							
	M	/	/	/							
24c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
25c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
26c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
27c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
28c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
29c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
30c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
31c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
32c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
33c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
34c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
35c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
36c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
37c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
38c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
39c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
40c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
41c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/

Legends: *Withdrawal*

Appendix 3-1/5

INVESTIGATIONAL PRODUCT: F3320 – Ref. F3320/RD0224E17 – Batch: 022E017221012H
SKIN EXAMINATION AND QUESTIONING DURING THE INDUCTION PHASE

Test subjects reference	Type of reaction	Experimental times									
		D1	D3	D5	D8	D10	D12	D15	D17	D19	D22
42c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
42c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
44c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
45c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
46c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
47c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
48c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
49c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
50c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
51c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
52c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
53c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
54c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
55c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
56c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/

Appendix 3-2/1

INVESTIGATIONAL PRODUCT: F3320 – Ref. F3320/RD0224E17 – Batch: 022E017221012H
SKIN EXAMINATION AND QUESTIONING DURING THE CHALLENGE PHASE

***E: Erythema**: **0** = no visible erythema, **0.5** = very slight erythema – barely perceptible, **1** = mild erythema – faint pink, **2** = moderate erythema – well defined, **3** = severe erythema, **4** = caustic effect – erosive aspect and/or necrotic aspect*
d= diffuse / p = punctuated / peri = peripheral

***M: Additional comments/Others reactions: H or Oe** = Homogeneous infiltration / oedema, **P** = Papules, **V** = Vesicles, **B** = Bullae, **Pe** = Petechiae, **S:** Spreading beyond the patch, **SV** = Soap effect (shiny skin with possibly wrinkles), **F** = Fissuring , **D** = Desquamation, **Dr** = Dryness, **C** = Skin coloration, hyperpigmentation, **HY** = Hypopigmentation, **Fr** = Follicular reaction, **NA** = Product not applied, **T**= Tape reaction, **I** = Itching at the test site, **Cr** = Exsudation and/or Surface encrustation, **Sc** = Scab, **Pr** = Pruritus, **He** = Heating, **Pu** = Pustules, * = Additional free comments, **N9G** = No 9th grade, **Abs or "–"** = Subject absent, **MU** = Make-up patch*

/: no reaction

***A: ICDRG scale**: **IR** = Irritation reaction, **-** = No allergic reaction, **?+ =** Doubtful reaction (only slight erythema), **(+) =** Weak positive reaction (without vesicle): slight erythema and infiltration with presence of small papular elevations, possibly papules, **(++) =** Strong positive reaction: erythema, papules, vesicles, infiltration, **(+++) =** Extreme positive reaction: intense erythema, oedema, coalescent vesicles (bullae)*

Test subjects reference	Type of reaction	Experimental times					
		Induction site			Virgin site		
		D37	D39	D41	D37	D39	D41
1a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
2a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
3a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
4a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
5a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
6a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
7a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
8a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
9a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
10a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
11a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
12a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
13a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					

Appendix 3-2/2

INVESTIGATIONAL PRODUCT: F3320 – Ref. F3320/RD0224E17 – Batch: 022E017221012H
SKIN EXAMINATION AND QUESTIONING DURING THE CHALLENGE PHASE

Test subjects reference	Type of reaction	Experimental times					
		Induction site			Virgin site		
		D37	D39	D41	D37	D39	D41
14a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
15a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
16a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
17a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
18a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
19a	E						
	M						
	A						
20a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
21a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
22a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
23a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
24a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
25a	E						
	M						
	A						
26a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
27a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
28a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
29a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					

Legends: *Withdrawal*

Appendix 3-2/3

INVESTIGATIONAL PRODUCT: F3320 – Ref. F3320/RD0224E17 – Batch: 022E017221012H
SKIN EXAMINATION AND QUESTIONING DURING THE CHALLENGE PHASE

Test subjects reference	Type of reaction	Experimental times					
		Induction site			Virgin site		
		D37	D39	D41	D37	D39	D41
30a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
31a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
32a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
33a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
34a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
35a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
36a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
37a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
38a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
39a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
40a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
41a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
42a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
43a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
44a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
45a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					

Appendix 3-2/4

INVESTIGATIONAL PRODUCT: F3320 – Ref. F3320/RD0224E17 – Batch: 022E017221012H
SKIN EXAMINATION AND QUESTIONING DURING THE CHALLENGE PHASE

Test subjects reference	Type of reaction	Experimental times					
		Induction site			Virgin site		
		D37	D39	D41	D37	D39	D41
46a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
47a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
48a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
49a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
50a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
51a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
52a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
53a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
54a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
55a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
56a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
1c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
2c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
3c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
4c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
5c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
6c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					

Appendix 3-2/5

INVESTIGATIONAL PRODUCT: F3320 – Ref. F3320/RD0224E17 – Batch: 022E017221012H
SKIN EXAMINATION AND QUESTIONING DURING THE CHALLENGE PHASE

Test subjects reference	Type of reaction	Experimental times					
		Induction site			Virgin site		
		D37	D39	D41	D37	D39	D41
7c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
8c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
9c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
10c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
11c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
12c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
13c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
14c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
15c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
16c	E						
	M						
	A						
17c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
18c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
19c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
20c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
21c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
22c	E						
	M						
	A						
23c	E						
	M						
	A						

Legends: *Withdrawal*

Appendix 3-2/6

INVESTIGATIONAL PRODUCT: F3320 – Ref. F3320/RD0224E17 – Batch: 022E017221012H
SKIN EXAMINATION AND QUESTIONING DURING THE CHALLENGE PHASE

Test subjects reference	Type of reaction	Experimental times					
		Induction site			Virgin site		
		D37	D39	D41	D37	D39	D41
24c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
25c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
26c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
27c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
28c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
29c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
30c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
31c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
32c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
33c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
34c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
35c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
36c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
37c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
38c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
39c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					

Appendix 3-2/7

INVESTIGATIONAL PRODUCT: F3320 – Ref. F3320/RD0224E17 – Batch: 022E017221012H
SKIN EXAMINATION AND QUESTIONING DURING THE CHALLENGE PHASE

Test subjects reference	Type of reaction	Experimental times					
		Induction site			Virgin site		
		D37	D39	D41	D37	D39	D41
40c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
41c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
42c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
43c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
44c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
45c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
46c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
47c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
48c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
49c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
50c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
51c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
52c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
53c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
54c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
55c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
56c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					

Appendix 4-1/1

CONTROL PRODUCT: DISTILLED WATER
SKIN EXAMINATION AND QUESTIONING DURING THE INDUCTION PHASE

***E: Erythema**: **0** = no visible erythema, **0.5** = very slight erythema – barely perceptible, **1** = mild erythema – faint pink, **2** = moderate erythema – well defined, **3** = severe erythema, **4** = caustic effect – erosive aspect and/or necrotic aspect*
d= diffuse / p = punctuated / peri = peripheral

***M: Additional comments/Others reactions: H or Oe** = Homogeneous infiltration / oedema, **P** = Papules, **V** = Vesicles, **B** = Bullae, **Pe** = Petechiae, **S:** Spreading beyond the patch, **SV** = Soap effect (shiny skin with possibly wrinkles), **F** = Fissuring , **D** = Desquamation, **Dr** = Dryness, **C** = Skin coloration, hyperpigmentation, **HY** = Hypopigmentation, **Fr** = Follicular reaction, **NA** = Product not applied, **T**= Tape reaction, **I** = Itching at the test site, **Cr** = Exsudation and/or Surface encrustation, **Sc** = Scab, **Pr** = Pruritus, **He** = Heating, **Pu** = Pustules, * = Additional free comments, **N9G** = No 9th grade, **Abs or "–"** = Subject absent, **MU** = Make-up patch*

/: no reaction

Test subjects reference	Type of reaction	Experimental times									
		D1	D3	D5	D8	D10	D12	D15	D17	D19	D22
1a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
2a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
3a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
4a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
5a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
6a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
7a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
8a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
9a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
10a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
11a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
12a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
13a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
14a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
15a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
16a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
17a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
18a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
19a	E	0	0	0	0						
	M	/	/	/	/						
20a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/

Legends: *Withdrawal*

Appendix 4-1/2

CONTROL PRODUCT: DISTILLED WATER
SKIN EXAMINATION AND QUESTIONING DURING THE INDUCTION PHASE

Test subjects reference	Type of reaction	Experimental times									
		D1	D3	D5	D8	D10	D12	D15	D17	D19	D22
21a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
22a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
23a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
24a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
25a	E	0	0								
	M	/	/								
26a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
27a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
28a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
29a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
30a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
31a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
32a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
33a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
34a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
35a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
36a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
37a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
38a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
39a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
40a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
41a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
42a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
43a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
44a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/

Legends: *Withdrawal*

Appendix 4-1/3

CONTROL PRODUCT: DISTILLED WATER
SKIN EXAMINATION AND QUESTIONING DURING THE INDUCTION PHASE

Test subjects reference	Type of reaction	Experimental times									
		D1	D3	D5	D8	D10	D12	D15	D17	D19	D22
45a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
46a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
47a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
48a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
49a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
50a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
51a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
52a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
53a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
54a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
55a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
56a	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
1c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
2c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
3c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
4c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
5c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
6c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
7c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
8c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
9c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
10c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
11c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
12c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
13c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
14c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
15c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/

Appendix 4-1/4

CONTROL PRODUCT: DISTILLED WATER
SKIN EXAMINATION AND QUESTIONING DURING THE INDUCTION PHASE

Test subjects reference	Type of reaction	Experimental times									
		D1	D3	D5	D8	D10	D12	D15	D17	D19	D22
16c	E	0	0	0	0						
	M	/	/	/	/						
17c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
18c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
19c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
20c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
21c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
22c	E	0	0	0							
	M	/	/	/							
23c	E	0	0	0							
	M	/	/	/							
24c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
25c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
26c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
27c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
28c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
29c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
30c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
31c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
32c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
33c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
34c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
35c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
36c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
37c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
38c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
39c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
40c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
41c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/

Legends: *Withdrawal*

Appendix 4-1/5

CONTROL PRODUCT: DISTILLED WATER
SKIN EXAMINATION AND QUESTIONING DURING THE INDUCTION PHASE

Test subjects reference	Type of reaction	Experimental times									
		D1	D3	D5	D8	D10	D12	D15	D17	D19	D22
42c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
42c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
44c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
45c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
46c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
47c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
48c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
49c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
50c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
51c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
52c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
53c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
54c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
55c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/
56c	E	0	0	0	0	0	0	0	0	0	0
	M	/	/	/	/	/	/	/	/	/	/

Appendix 4-2/1

CONTROL PRODUCT: DISTILLED WATER
SKIN EXAMINATION AND QUESTIONING DURING THE CHALLENGE PHASE

***E: Erythema**: **0** = no visible erythema, **0.5** = very slight erythema – barely perceptible, **1** = mild erythema – faint pink, **2** = moderate erythema – well defined, **3** = severe erythema, **4** = caustic effect – erosive aspect and/or necrotic aspect*
d= diffuse / p = punctuated / peri = peripheral

***M: Additional comments/Others reactions: H or Oe** = Homogeneous infiltration / oedema, **P** = Papules, **V** = Vesicles, **B** = Bullae, **Pe** = Petechiae, **S:** Spreading beyond the patch, **SV** = Soap effect (shiny skin with possibly wrinkles), **F** = Fissuring , **D** = Desquamation, **Dr** = Dryness, **C** = Skin coloration, hyperpigmentation, **HY** = Hypopigmentation, **Fr** = Follicular reaction, **NA** = Product not applied, **T**= Tape reaction, **I** = Itching at the test site, **Cr** = Exsudation and/or Surface encrustation, **Sc** = Scab, **Pr** = Pruritus, **He** = Heating, **Pu** = Pustules, * = Additional free comments, **N9G** = No 9th grade, **Abs or "–"** = Subject absent, **MU** = Make-up patch*

/: no reaction

***A: ICDRG scale**: **IR** = Irritation reaction, **-** = No allergic reaction, **?+ =** Doubtful reaction (only slight erythema), **(+) =** Weak positive reaction (without vesicle): slight erythema and infiltration with presence of small papular elevations, possibly papules, **(++) =** Strong positive reaction: erythema, papules, vesicles, infiltration, **(+++) =** Extreme positive reaction: intense erythema, oedema, coalescent vesicles (bullae)*

Test subjects reference	Type of reaction	Experimental times					
		Induction site			Virgin site		
		D37	D39	D41	D37	D39	D41
1a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
2a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
3a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
4a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
5a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
6a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
7a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
8a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
9a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
10a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
11a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
12a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
13a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					

Appendix 4-2/2

CONTROL PRODUCT: DISTILLED WATER
SKIN EXAMINATION AND QUESTIONING DURING THE CHALLENGE PHASE

Test subjects reference	Type of reaction	Experimental times					
		Induction site			Virgin site		
		D37	D39	D41	D37	D39	D41
14a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
15a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
16a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
17a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
18a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
19a	E						
	M						
	A						
20a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
21a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
22a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
23a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
24a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
25a	E						
	M						
	A						
26a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
27a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
28a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
29a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					

Legends: *Withdrawal*

Appendix 4-2/3

CONTROL PRODUCT: DISTILLED WATER
SKIN EXAMINATION AND QUESTIONING DURING THE CHALLENGE PHASE

Test subjects reference	Type of reaction	Experimental times					
		Induction site			Virgin site		
		D37	D39	D41	D37	D39	D41
30a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
31a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
32a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
33a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
34a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
35a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
36a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
37a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
38a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
39a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
40a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
41a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
42a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
43a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
44a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
45a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					

Appendix 4-2/4

CONTROL PRODUCT: DISTILLED WATER
SKIN EXAMINATION AND QUESTIONING DURING THE CHALLENGE PHASE

Test subjects reference	Type of reaction	Experimental times					
		Induction site			Virgin site		
		D37	D39	D41	D37	D39	D41
46a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
47a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
48a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
49a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
50a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
51a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
52a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
53a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
54a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
55a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
56a	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
1c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
2c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
3c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
4c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
5c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
6c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					

Appendix 4-2/5

CONTROL PRODUCT: DISTILLED WATER
SKIN EXAMINATION AND QUESTIONING DURING THE CHALLENGE PHASE

Test subjects reference	Type of reaction	Experimental times					
		Induction site			Virgin site		
		D37	D39	D41	D37	D39	D41
7c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
8c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
9c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
10c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
11c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
12c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
13c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
14c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
15c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
16c	E						
	M						
	A						
17c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
18c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
19c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
20c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
21c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
22c	E						
	M						
	A						
23c	E						
	M						
	A						

Legends: *Withdrawal*

Appendix 4-2/6

CONTROL PRODUCT: DISTILLED WATER
SKIN EXAMINATION AND QUESTIONING DURING THE CHALLENGE PHASE

Test subjects reference	Type of reaction	Experimental times					
		Induction site			Virgin site		
		D37	D39	D41	D37	D39	D41
24c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
25c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
26c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
27c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
28c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
29c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
30c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
31c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
32c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
33c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
34c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
35c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
36c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
37c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
38c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
39c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					

Appendix 4-2/7

CONTROL PRODUCT: DISTILLED WATER
SKIN EXAMINATION AND QUESTIONING DURING THE CHALLENGE PHASE

Test subjects reference	Type of reaction	Experimental times					
		Induction site			Virgin site		
		D37	D39	D41	D37	D39	D41
40c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
41c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
42c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
43c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
44c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
45c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
46c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
47c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
48c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
49c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
50c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
51c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
52c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
53c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
54c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
55c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					
56c	E	0	0	0	0	0	0
	M	/	/	/	/	/	/
	A	-					