STUDY REFERENCE: VV_CC-HRIPT/50D1_699_21_001

Study Report - Version nº 2

ASSESSMENT IN HUMANS OF THE CUTANEOUS COMPATIBILITY AND THE ABSENCE OF ALLERGENIC POTENTIAL OF A COSMETIC PRODUCT AFTER REPEATED UNDER PATCH APPLICATIONS WITH DERMATOLOGICAL CONTROL

HUMAN REPEATED INSULT PATCH TEST (HRIPT)

SPONSOR: NANO Z COATINGS LTD
TESTED ELEMENT: *HWC - DRY CLOTH SOAKED IN SOAP*
REFERENCE: -

Madrid, October 15th, 2021

All the changes on the present report respect to the previous version are indicated in italics

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1. SYNOPSYS

SPONSOR	NANO Z COATINGS LTD
Tested product	Product name: *HWC - DRY CLOTH SOAKED IN SOAP* Product reference: - Batch: 2923
Testing Facility	ZURKO RESEARCH S.L Avenida de la Osa Mayor, 4. 28023, Madrid (España) Tel: (+34) 91.521.15.88
Technical team	Laboratory director: María Barbero Calderón, pharmacist Tolerance Department manager: Jesús González Cuartero, pharmacist Researcher: Jesús González Cuartero, pharmacist Technician: Ainhoa Yepes Agudo, Inés Rodríguez de Roa Peñarando Dermatologist: Javier Pedraz Muñoz. Medical license number: 283706434
Study code	VV_CC-HRIPT/50D1_699_21_001
Panelists	Number of panelists enrolled: 61 Gender: both Age range: 18-70 years Skin type: sensitive skin according to center criteria Number of panelists completed: 52
Test area	Upper back
Application	Duration: 40 days Frequency: repeated applications under patch
Test period	August 30th, 2021 –October 7th, 2021 *Final report version no. 1: October 14th, 2021*
Test parameters	Cutaneous evaluation of erythema and oedema
Design of study	Day 1, 3, 5, 8, 10, 12, 15, 17, 19, 36 – Sample preparation and application Day 3, 5, 8, 10, 12, 15, 17, 19, 22, 36, 38, 39, 40 – Clinical and dermatological evaluation
Evaluation	Cutaneous Mean Irritation Index (M.I.I.) and allergenicity

Results:

Under adopted experimental conditions, the product, ***HWC - DRY CLOTH SOAKED IN SOAP*****,** reference: **-** has **Intermediate Cutaneous Compatibility, 31%** of the panelists showed some kind of erythema or oedema reaction to the product during the induction phase.

Under the experimental conditions adopted, **No allergenicity** has been observed in any of the tested panelists.

2. OBJECTIVE AND PRINCIPLE OF THE STUDY

This study had as an objective verifying the cutaneous compatibility and the absence of allergenic potential of a cosmetic product after repeated skin applications, under exaggerated experimental conditions.

The product was applied to the skin under patch 9 times during 3 consecutive weeks. After a minimum of two weeks of rest with the patch application, the product was reapplied under patch in duplicate sites.

The compatibility of the product with the skin was verified, after removing the patch, and through visual examination of the experimental area, by the responsible technical expert and the dermatologist in charge of the study.

The method used is an adaptation of the one described by Marzulli and Maibach (Marzulli F.N., Maibach H.I., Contact allergy: predictive testing in man, Contact dermatitis, 1976, 2, pp.1-17).

The study was carried out following general conditions in Zurko Research, established for the execution of study project on humans (Structure and Content of Clinical Study Reports from ICH Harmonised Tripartite Guideline; Guideline for good clinical practice E6 (R2) of June 14th 2017, EMA/CHMP/ICH/135/1995 of May 1st 1996, European Parliament and Council Guideline 2001/20/CE – May 1st 2001).

The negative control excluded false positives.

3. PANELISTS

3.1. Ethical aspects

Each participating panelist in the study was previously informed about the type and the procedures of the study and signed an Informed Consent Form before the beginning of the study.

3.2. Specific inclusion and exclusion criteria

The specific inclusion criteria, defined in the protocol, were as follow:

- Age: 18-70 years old
- Photo-type (Fitzpatrick): I to IV
- Skin type: sensitive skin according to center criteria

The specific exclusion criteria, defined in the protocol, were as follow:

- Cutaneous marks on the experimental area that could interfere with the evaluation of the skin reactions (pigmentation disruptions, scars, excessive hair areas, excessive freckles and moles, solar skin burns, tattoos…)
- Injuries, pathologies or infection in the experimental area
- Eczematous reaction which has not fully disappeared, scar or pigmentation complications from previous studies in the experimental area

- Have the intention of bathing in bathtub, sea or pool or going to sauna or Turkish bath during the study
- Intense sun exposure or UV rays during the study, or having sunbathed or UV rays during the month prior to the study on the test area
- Carrying out a treatment containing acid vitamin A or its by-products, during the 3 months previous to the study
- Carrying out a treatment containing topical corticoids, on the experimental area during the 8 days previous to the beginning of the study
- Carrying out a treatment with any medicine for psoriasis or vitiligo, during the month previous to the study
- Having the intention to be vaccinated during the study or have been vaccinated during the 3 weeks previous to the study
- Being pregnant or breastfeeding period
- Allergies to metals
- Reactivity to medical tape
- Participation during the previous 30 days in any study under exaggerated conditions (under a patch).

Information about the participating panelist is included in Annex I.

4. METHODOLOGY

4.1. Criteria for application the product

Type of product: textile fabric.

Product preparation: the sample is cut in pieces of 0,25 cm^2.

Applied quantity: a piece of 0,25 cm^2 prepared over occlusive patch (Finn Chamber Aqua® occlusive patch).

4.2. Chronology of the study

Test duration: 6-8 consecutive weeks (40 days) without considering the re-challenge phase.

First phase: Induction Phase lasts three weeks:

- Application of the product under patch on days 1, 3, 5, 8, 10, 12, 15, 17, 19.
- Patch removal by the panelist at home on days 2, 4, 6, 9, 11, 13, 16, 18, 20 (after 24 hours of the application of the patch).
- Skin examination at 24 hours after patch removal on days 3, 5, 10, 12, 17, 19.
- Skin examination at 48 hours after patch removal on days 8, 15, 22.
- If excessive irritation develops anywhere, the product that cause the irritation is not reapplied and the panelist is excluded from the study.

Second phase: Rest phase. The duration was minimum 2 consecutive weeks and maximum 4. In this phase the product under study was not applied.

Third phase: Challenge or **Memory phase**: 1 week.

- Skin examination and application of the product under patch on Monday. The patch is applied in two areas, the induction area and the virgin area
- Patch removal by the panelist him/herself at home after 24 hours of the application.
- Skin examination 24 and 48 hours after the patch removal. 72 hours after the patch removal the skin is examined in those panelists who were reactive during the memory phase. For those panelists in which no reaction was observed, a negative result is assumed also on 72 hours.

Alternatively, the fourth phase: **Re-challenge phase.** It can be performed between 4 and 12 weeks after the initial challenge phase. Panelists who exhibit in challenge phase an inconclusive response and/or more information about challenge response is needed, a re-challenge can be performed between 4 and 12 weeks after the initial challenge phase. The experimental procedure is the same that challenge phase.

4.3. Experimental procedure

		Day
Induction	Informed Consent Form signature	1
	Specific inclusion and exclusion criteria	1
	Patch application	1, 3, 5, 8, 10, 12, 15, 17, 19
	Evaluation after 24 hours of the patch removal by the panelists their selves and before reapply the patch	3, 5, 8, 10, 12, 15, 17, 19, 22
Two weeks rest		
Challenge	Duplicate patch application	36
	Evaluation after 24 hours of the patch removal	38, 39, 40

Each day of evaluation the product is assigned an erythema score according the following scale:

Score	Assessment of reaction	PARAMETERS EVALUATED	
		Erythema (E)	Oedema (OE)
0	Absence	No visible erythema	No visible oedema
1	Slight	Slight erythema (quiet pinked coloration of the complete tested area or rather visible on one part of the tested area)	Slight oedema (palpable and visible)
2	Moderate	Obvious erythema (clear erythema covering all of the tested area)	Obvious oedema with or without vesicle/s
3	Severe	Intense erythema (severe erythema covering all the tested area or erythema diffusing outside the tested area)	Intense oedema (extended area outside the tested area) with or without vesicle/s or blister/s

Table 1. Clinical Examination of Erythema and Oedema Scoring

Other elevated responses could be observed, if present, are graded as independent responses:

- **P** Papules – many small, red, solid elevations; surface of reaction has granular feeling
- **PU** Pustules – small, circumscribed, elevated and inflamed skin lesions, with pus at its centre.
- **V** Vesicles – small, circumscribed elevations having translucent surfaces so that fluid is visible (blister – like). Vesicles are no larger than 0.5 cm in diameter.
- **B** Bullae – vesicles with a diameter> 0.5 cm; vesicles may coalesce to form one or a few large blisters that fill the patch site.

Other responses could be observed:

- **S** Spreading – evidence of the reaction beyond the patch area
- **W** Weeping – evidence of release of fluid from a vesicular or bullous reaction
- **A** Marked reaction to adhesive (patch relocated).
- **X** Succeeding patch not applied and succeeding grade is for residual reaction

4.4. Interpretation of Results

The interpretation of the results of an HRIPT was carried out on a case-by-case basis using immunological principles, general interpretation guidelines and experience. The standard scoring scale used to interpret skin responses was provided in Table 1 and Table 2.

The following guidelines have been developed for the interpretation of reactions that may occur during an HRIPT.

- Skin sensitization reactions are most frequently erythematous, papular and edematous. Conversely, primary irritation reactions (unless severe), are generally erythematous only. An irritation reaction is usually uniform with a well-defined border, whereas an allergic response (especially if weak) is typically non-uniform and has an irregular border, and a strong response may spread beyond the patch site.
- Responses which are more severe at challenge than in early induction are suggestive of induction of skin sensitization.
- Responses confined to induction site during challenge phase are suggestive of irritation. True allergic reactions in challenge phase will occur at both site (induction site and virgin site) and persist through 2 delayed scorings at least 24 hours apart. However, unilateral allergic reactions can sometimes be observed. For this reason, all reactions considered suggestive of induction of skin sensitization should be followed up, for example, by re-challenge.
- Responses that increase or maintain severity with time from the 48 to 96 hours challenge gradings are presumptive of skin sensitization. Those that subside from the 48 to 96 hours grading period are generally considered to be irritant in nature.
- Edematous reactions that occur and persist during the latter part of the induction phase and the challenge phase are indicative of induced skin sensitization and should be confirmed by re-challenge.

- Persistent skin responses with papules and/or edema occurring in week 1 of induction suggest pre-existing skin sensitization. Similar reactions that occur later in induction suggest induction of skin sensitization by the test material.
- Reactions and reaction patterns that are suggestive of allergic reactions or questionable/equivocal reactions should be verified through appropriate re-challenge procedures.
- The reactions of any panelist(s) in question should always be compared with those of all other exposed panelists. Except in rare instances, allergic reactivity occurs in only a very small number of subjects, while irritation occurs more widely throughout the exposed population.

The HRIPT objective was to verify the absence of allergenic potential and the skin sensitization of a cosmetic product according to results from Induction phase and Challenge Phase. In parallel, a conclusion of the induction phase related to the cutaneous compatibility, could be drawn according to the calculation of the Mean Irritation Index (M.I.I.) global which was obtained according to average of the calculation of the daily Mean Irritation Index:

$$\textbf{Daily M. I. I.} = \frac{\sum(\bar{\textbf{x}}\ \textbf{of the erythema and oedema grade})}{\textbf{Number of panelists}}$$

The obtained index is used to classify the studied cosmetic product according to the following scale:

M.I.I.	Product Classification
M.I.I.=0.000	Non-Irritating (NI)/Very Good Cutaneous Compatibility
M.I.I. <0.022	Non-Irritating (NI) / Good Cutaneous Compatibility
0.022≤ M.I.I. <0.055	Slightly Irritating (SI) / Intermediate Cutaneous Compatibility
0.055≤ M.I.I. <0.111	Moderately Irritating (NI) / Bad Cutaneous Compatibility
M.I.I. ≥0.111	Irritating (I) / Very Bad Cutaneous Compatibility

Table 2. Cutaneous compatibility cosmetic product classification index

5. RESULTS

The individual reading results are presented in Annex II.

Next table showed the Global M.I.I. after induction phase.

M.I.I.	Results	No. reactive panelists	% reactive panelists
0,033	Slightly Irritating (SI)/Intermediate Cutaneous Compatibility	18	31%

Next table shows the results of Challenge or Memory phase:

Challenge (Memory phase)	No. reactive panelists		% reactive panelists	
	Induction area	Virgin area	Induction area	Virgin area
	0	0	0%	0

The individual reading results are presented in Annex III.

Allergenicity result:

The allergenicity result was set up from the results obtained in the induction phase and in the memory phase (induction area and virgin area).

Results	No. panelists showing some kind of allergic reaction	% reactive panelists
	0	0%

6. SAMPLES AND DOCUMENTS TO BE STORED

The following documentation relating to the study will be stored in the facilities of Zurko Research following the provisions of ISO 9001:2015:

- Informed Consent Forms signed
- Study protocol and its modifications (signed)
- Primary data
- Final report and its modifications (signed)
- Documents provided by the sponsor

The documents will be stored during 5 years. After 5 years the sponsor will be asked about the possibility of extension because of the commercialization of the tested element.

A sample of the evaluated product (sufficient quantity for the execution of the study) will be stored in the Zurko Research samples library for 1 year from the start date of the study.

7. BIBLIOGRAPHICAL REFERENCES

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5. Nueva Clasificación de tipos piel y sus implicaciones en Dermatología Cosmética. Revisión Dermatología Venezolana. Vol. 43, Nº 4, 2005. Leslie Baumann, Sadegh Amini, Eduardo Weiss.

SIGNATURES

The undersigned declare that this study has been carried out in the essence of the Clinical Good Practices (Guideline for good clinical practice E6 (R2) of June 14th 2017, EMA/CHMP/ICH/135/1995 of May 1st 1996, European Parliament and Council Guideline 2001/20/CE – May 1st 2001).

The results here presented reflect accurately and completely the raw data of the study.

Researcher: I, the undersigned, Jesús González Cuartero, declare that this study has been **carried out** under my responsibility.

Jesús González Cuartero

Dermatology Team: Zurko's dermatology team, led by the dermatologist Javier Pedraz (medical license number: 283706434), and Natalia Zawierta, as adjunct dermatologist, declare that this study has been **reviewed** under their responsibility. In representation,

ZAWIERTA NATALIA MARIA - Y3942816D

Annex I: Information relating to panelists

Panelists		Age	Sex	Skin type	Photo-type
Ref.	Acronym				
1	V01	59	F	S	III
2	V02	51	F	S	IV
3	V03	21	F	S	II
4	V04	65	F	S	IV
5	V05	29	M	S	II
6	V06	51	F	S	II
7	V07	51	F	S	II
8	V09	31	F	S	II
9	V11	58	M	S	IV
10	V13	40	F	S	III
11	V14	33	F	S	II
12	V15	51	F	S	II
13	V16	30	F	S	IV
14	V17	23	M	S	II
15	V18	18	F	S	III
16	V19	45	F	S	IV
17	V21	36	M	S	III
18	V22	28	F	S	III
19	V23	21	F	S	III
20	V24	44	F	S	IV
21	V26	31	M	S	II
22	V27	66	M	S	III
23	V28	39	F	S	III
24	V30	51	F	S	II
25	V32	52	F	S	IV
26	V33	26	F	S	IV

27	V34	48	M	S	III
28	V35	50	M	S	III
29	V36	42	F	S	IV
30	V37	68	F	S	II
31	V38	54	F	S	II
32	V39	63	F	S	III
33	V40	41	F	S	II
34	V41	62	F	S	III
35	V42	63	F	S	III
36	V43	43	F	S	III
37	V44	35	F	S	III
38	V45	55	M	S	III
39	V46	51	F	S	III
40	V47	25	F	S	III
41	V48	36	F	S	III
42	V49	54	F	S	III
43	V50	22	F	S	III
44	V53	56	F	S	III
45	V54	31	F	S	III
46	V55	36	F	S	IV
47	V56	26	F	S	III
48	V57	40	F	S	IV
49	V58	22	F	S	III
50	V59	50	F	S	II
51	V60	55	F	S	III
52	V61	45	F	S	III

M: male, F: female; R: non-sensitive, S: sensitive

Two panelists (V08, V51) left the study due to reasons unrelated to it. Seven exclusions (V10, V12, V20, V25, V29, V31, V52) were decided for the researcher due to exaggerated reaction to the product.

Annex II: Individual results from Induction phase

Panelists		Reaction in Induction Phase (according to Table 1)																								
		DAY 3			DAY 5			DAY 8			DAY 10			DAY 12			DAY 15			DAY 17			DAY 19			DAY 22		
Ref	Acr.	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot
1	V01	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	V02	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	V03	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	V04	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
5	V05	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
6	V06	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7	V07	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8	V09	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9	V10	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	2	0	0	/	/	/	/	/	/	/	/	/
10	V11	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
11	V12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	/	/	/	/	/	/	/	/	/
12	V13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13	V14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14	V15	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15	V16	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16	V17	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Panelists		Reaction in Induction Phase (according to Table 1)																										
		DAY 3			DAY 5			DAY 8			DAY 10			DAY 12			DAY 15			DAY 17			DAY 19			DAY 22		
Ref	Acr.	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot
17	V18	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
18	V19	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
19	V20	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	1	0	0
20	V21	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
21	V22	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
22	V23	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
23	V24	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
24	V25	1	0	0	0	0	0	2	0	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
25	V26	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
26	V27	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
27	V28	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
28	V29	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	1	0	/	/	/	/	/	/
29	V30	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
30	V31	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	/	/	/	/	/	/	/	/	/
31	V32	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
32	V33	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
33	V34	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Panelists		Reaction in Induction Phase (according to Table 1)																								
		DAY 3			DAY 5			DAY 8			DAY 10			DAY 12			DAY 15			DAY 17			DAY 19			DAY 22		
Ref	Acr.	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot
34	V35	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
35	V36	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
36	V37	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
37	V38	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
38	V39	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
39	V40	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
40	V41	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0
41	V42	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
42	V43	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
43	V44	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
44	V45	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
45	V46	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
46	V47	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
47	V48	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
48	V49	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
49	V50	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0
50	V52	0	0	0	0	0	0	0	0	0	3	0	0	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/

Panelists		Reaction in Induction Phase (according to Table 1)																										
		DAY 3			DAY 5			DAY 8			DAY 10			DAY 12			DAY 15			DAY 17			DAY 19			DAY 22		
Ref	Acr.	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot	E	OE	Ot
51	V53	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
52	V54	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0
53	V55	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
54	V56	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
55	V57	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
56	V58	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
57	V59	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
58	V60	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0
59	V61	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Daily M.I.I.		**0,008**			**0,000**			**0,017**			**0,026**			**0,018**			**0,088**			**0,065**			**0,047**			**0,047**		
Global M.I.I.		**0,033**																										

0: non-visible erythema, 1: slight erythema, 2: moderate erythema, 3: intense erythema

P: papules, PU: pustules, V: vesicles, B: bullae, S: spreading, W: weeping, X: residual pigmentation

Annex III: Individual Results from Challenge phase

Panelists		Reaction in Challenge Memory phase								
		Induction Area				Virgin Area				Allergeniciy Result (-/+)
Ref.	Acronym	D36	D38	D39	D40	D36	D38	D39	D40	
1	V01	0	0	0	0	0	0	0	0	-
2	V02	0	0	0	0	0	0	0	0	-
3	V03	0	0	0	0	0	0	0	0	-
4	V04	0	0	0	0	0	0	0	0	-
5	V05	0	0	0	0	0	0	0	0	-
6	V06	0	0	0	0	0	0	0	0	-
7	V07	0	0	0	0	0	0	0	0	-
8	V09	0	0	0	0	0	0	0	0	-
9	V11	0	0	0	0	0	0	0	0	-
10	V13	0	0	0	0	0	0	0	0	-
11	V14	0	0	0	0	0	0	0	0	-
12	V15	0	0	0	0	0	0	0	0	-
13	V16	0	0	0	0	0	0	0	0	-
14	V17	0	0	0	0	0	0	0	0	-
15	V18	0	0	0	0	0	0	0	0	-
16	V19	0	0	0	0	0	0	0	0	-
17	V21	0	0	0	0	0	0	0	0	-
18	V22	0	0	0	0	0	0	0	0	-
19	V23	0	0	0	0	0	0	0	0	-
20	V24	0	0	0	0	0	0	0	0	-
21	V26	0	0	0	0	0	0	0	0	-
22	V27	0	0	0	0	0	0	0	0	-
23	V28	0	0	0	0	0	0	0	0	-
24	V30	0	0	0	0	0	0	0	0	-
25	V32	0	0	0	0	0	0	0	0	-
26	V33	0	0	0	0	0	0	0	0	-
27	V34	0	0	0	0	0	0	0	0	-
28	V35	0	0	0	0	0	0	0	0	-
29	V36	0	0	0	0	0	0	0	0	-

Panelists		Reaction in Challenge Memory phase								
		Induction Area				Virgin Area				Allergeniciy Result (-/+)
Ref.	Acronym	D36	D38	D39	D40	D36	D38	D39	D40	
30	V37	0	0	0	0	0	0	0	0	-
31	V38	0	0	0	0	0	0	0	0	-
32	V39	0	0	0	0	0	0	0	0	-
33	V40	0	0	0	0	0	0	0	0	-
34	V41	0	0	0	0	0	0	0	0	-
35	V42	0	0	0	0	0	0	0	0	-
36	V43	0	0	0	0	0	0	0	0	-
37	V44	0	0	0	0	0	0	0	0	-
38	V45	0	0	0	0	0	0	0	0	-
39	V46	0	0	0	0	0	0	0	0	-
40	V47	0	0	0	0	0	0	0	0	-
41	V48	0	0	0	0	0	0	0	0	-
42	V49	0	0	0	0	0	0	0	0	-
43	V50	0	0	0	0	0	0	0	0	-
44	V53	0	0	0	0	0	0	0	0	-
45	V54	0	0	0	0	0	0	0	0	-
46	V55	0	0	0	0	0	0	0	0	-
47	V56	0	0	0	0	0	0	0	0	-
48	V57	0	0	0	0	0	0	0	0	-
49	V58	0	0	0	0	0	0	0	0	-
50	V59	0	0	0	0	0	0	0	0	-
51	V60	0	0	0	0	0	0	0	0	-
52	V61	0	0	0	0	0	0	0	0	-

0: non-visible erythema, 1: slight erythema, 2: moderate erythema, 3: intense erythema