Product
GEL NETTOYANT DOUX EASY TATOO
GEL NETTOYANT DOUX EASY PIERCING –
REF : CTG152136/0/02 CTG152138/0/02

Assessment of cutaneous compatibility of a cosmetic product after repeated applications on the area of the elbow bend for 5 consecutive days on stripped skin and unstripped skin under dermatological control - repeated open application test

(Clinical report on 11 adult volunteers)

Study code	:	**1.04.D.STR_5J**
Product code	:	**ID-16/11046**
Report date	:	**16/02/2017**

FAREVACARE
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CS 20235
77545 SAVIGNY LE TEMPLE
FRANCE

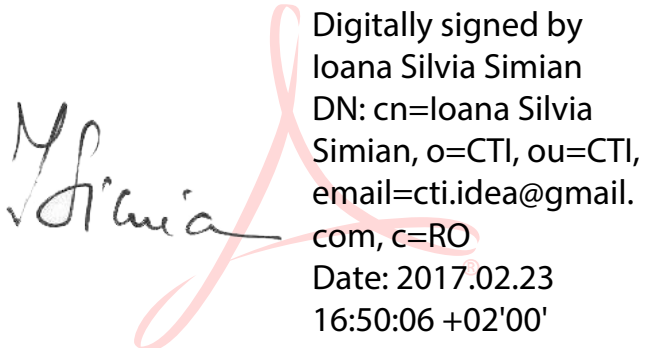
CONTENTS

AUTHENTICITY OF THE RESULTS

The study covered by this present report was carried out under my responsibility, in compliance with the experimental protocol and in the spirit of Good Clinical Practices. All observations and numerical data collected during this test are reported in the present document.

After rereading this report, I certify that these data are consistent with the factual results obtained,
Ioana Silvia SIMIAN, Dermatologist, Investigator.

Signature / date:



The generated data were audited by CTI's Quality Control.
This report was audited by IDEA Clinic's Quality Assurance.
It is considered to accurately reflect the generated data and current experimental protocols used complying with Good Clinical Practices.

Signature / date:

Noémie JOHANNY
Quality Assistant
2017.02.23 18:14:28 +01'00'
Emis par : CN=ChamberSign France - AC 1 étoile,
OU=0002 433702479, O=ChamberSign France, C=FR

1. PURPOSE OF THE STUDY

At the request of **FAREVACARE** company, we have assessed, after daily application on the elbow bend, on stripped and unstripped skin area, for 5 consecutive days, the skin compatibility of the cosmetic product:

GEL NETTOYANT DOUX EASY TATOO
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After applying 0.07 ml of the product at the centre, the volunteer bent his arms for 15 minutes in order to obtain an occlusive effect. 30 minutes after extending the arms, the investigator examined once again the treated and control sites.

2. INVESTIGATED PRODUCT

Name	**:**	GEL NETTOYANT DOUX EASY TATOO GEL NETTOYANT DOUX EASY PIERCING - REF : CTG152136/0/02 CTG152138/0/02
IDEA TESTS code	**:**	ID-16/11046
Batch number	**:**	161025D1
Aspect	**:**	Gel
Colour	**:**	Pale yellow
Product type	**:**	Finished cosmetic product
Product class	**:**	Hygiene
Storage conditions	**:**	Room temperature
Expiry date	**:**	25/10/2017
Packaging	**:**	Plastic bottle
Number of received samples	**:**	1

3. COURSE OF THE STUDY

The investigation was carried out from 30/01/2017 to 03/02/2017 at CTI, Street Iuliu Teodori, Number (no.) 1, Sector 5, 010221 BUCHAREST, Romania, according to the internal standard protocol 1.04.D.STR_5J (cf. annex 3).

4. VOLUNTEERS' CHARACTERISTICS

10 adult volunteers, from 18 to 70 years of age, with all type of body skin (elbow bend) and who usually apply an hygiene product for body, should be included in the study.

5. METHODOLOGY

Cf. Protocol n° 1.04.D.STR_5J (annex 3).

6. RESULTS – DISCUSSION

6.1. Results

11 adult volunteers (10 women and 1 man), with an average age of 53 years, between 25 and 66 years and with all type of body skin (elbow bend), participated in the study.

The results of the investigation are shown in the annexes to the present report.

Events during the study / protocol deviations

- Withdrawal during the investigation: 0
- Exclusion from the study: 0
- Errors in application plan: 0
- Restraints and restrictions were not complied with: 0
- Appointment dates were not complied with: 0
- Other events / deviations: 0

All the included volunteers were taken into account in the analysis.

6.2. Discussion

The results of the daily individual examinations from D1 to D5 before the application and 45 minutes after the application of the product are shown in annex 1.

The tables 1 and 2 show the result of the examinations on the treated and the control sites at T0 and T45min before the application and 45 minutes after the application of the product, from D1 to D5.

Table 1

Treated site ID-16/11046 : right elbow bend					
Days	**T 0**			**T 45 minutes**	
	Before stripping	**After stripping**	**Unstripped**	**Stripped**	**Unstripped**
D 1	2 dryness 0.5 2 dryness 1	6 erythemas 0.5 4 erythemas 1 2 dryness 0.5 2 dryness 1	2 dryness 0.5 2 dryness 1	3 erythemas 0.5 3 dryness 0.5	3 dryness 0.5
D 2	1 erythema 0.5 2 dryness 0.5 2 dryness 1	9 erythemas 0.5 2 erythemas 1 2 dryness 0.5 2 dryness 1	1 erythema 0.5 2 dryness 0.5 2 dryness 1	2 dryness 0.5	2 dryness 0.5
D 3	1 erythema 0.5 3 dryness 0.5 1 dryness 1	7 erythemas 0.5 4 erythemas 1 3 dryness 0.5 1 dryness 1	1 erythema 0.5 3 dryness 0.5 1 dryness 1	2 dryness 0.5	2 dryness 0.5
D 4	1 erythema 0.5 3 dryness 0.5	6 erythemas 0.5 5 erythemas 1 3 dryness 0.5	1 erythema 0.5 3 dryness 0.5	1 erythema 0.5	-
D 5	2 dryness 0.5	6 erythemas 0.5 4 erythemas 1 1 erythema 2 2 dryness 0.5	2 dryness 0.5	1 erythema 0.5	-
Sum	**1.5**	**38**	**1.5**	**2.5**	**0**
M.I.I.	**0.03**	**0.69**	**0.03**	**0.05**	**0**

Rating : 0.5 = very slight; 1 = slight; 2 = moderate; 3 = important

Table 2

Control site : left elbow bend					
Days	**T 0**			**T 45 minutes**	
	Before stripping	**After stripping**	**Unstripped**	**Stripped**	**Unstripped**
D 1	2 dryness 0.5 2 dryness 1	7 erythemas 0.5 3 erythemas 1 2 dryness 0.5 2 dryness 1	2 dryness 0.5 2 dryness 1	1 erythema 0.5 2 dryness 0.5 2 dryness 1	2 dryness 0.5 2 dryness 1
D 2	1 erythema 0.5 2 dryness 0.5 2 dryness 1	7 erythemas 0.5 3 erythemas 1 2 dryness 0.5 2 dryness 1	1 erythema 0.5 2 dryness 0.5 2 dryness 1	2 dryness 0.5 2 dryness 1	2 dryness 0.5 2 dryness 1
D 3	1 erythema 0.5 3 dryness 0.5 1 dryness 1	9 erythemas 0.5 2 erythemas 1 2 dryness 0.5 2 dryness 1	1 erythema 0.5 2 dryness 0.5 2 dryness 1	2 dryness 0.5 2 dryness 1	2 dryness 0.5 2 dryness 1
D 4	1 erythema 0.5 2 dryness 0.5 2 dryness 1	6 erythemas 0.5 4 erythemas 1 2 dryness 0.5 2 dryness 1	1 erythema 0.5 2 dryness 0.5 2 dryness 1	1 dryness 0.5 2 dryness 1	1 dryness 0.5 2 dryness 1
D 5	2 erythemas 0.5 2 dryness 0.5 2 dryness 1	5 erythemas 0.5 3 erythemas 1 1 erythema 2 2 dryness 0.5 2 dryness 1	1 erythema 0.5 2 dryness 0.5 2 dryness 1	2 dryness 0.5 2 dryness 1	2 dryness 0.5 2 dryness 1
Sum	**2.5**	**34**	**2**	**0.5**	**0**
M.I.I.	**0.05**	**0.62**	**0.04**	**0.01**	**0**

Rating : 0.5 = very slight; 1 = slight; 2 = moderate; 3 = important

In view of these results, after a 5 day repeated application period on the stripped site, the mean irritation index was equal to 0.05, superior to M.I.I of the control site (0.01) but judged as acceptable by the investigator.

According to the scale used for the interpretation, the product ID-16/11046 can be considered as non irritant for body skin.

7. CONCLUSION

Under the accepted experimental conditions, i.e., after daily application and stripping on the elbow bend of 11 adult volunteers (10 women and 1 man), with an average age of 53 years, between 25 and 66 years, with all type of body skin (elbow bend), the product:

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can be considered as non irritant for body skin, according to the scale used for the interpretation.

ANNEX 1

Volunteers' characteristics
Individual values of the dermatological examination from D1 to D5

Volunteers' characteristics
GEL NETTOYANT DOUX EASY TATOO
GEL NETTOYANT DOUX EASY PIERCING - REF : CTG152136/0/02 CTG152138/0/02

Inclusion no.	Initials	Sex	Age (years)	Skin type on body	Current treatments
1	SA-CA	F	47	Normal and non-sensitive	-
2	AP-MI	F	41	Normal and sensitive	-
3	EF-AN	F	36	Normal and non-sensitive	-
4	BA-DA	F	25	Normal and non-sensitive	-
5	CR-TA	F	55	Normal and sensitive	-
6	AN-LA	F	66	Dry and sensitive	-
7	SI-MI	M	63	Normal and non-sensitive	-
8	CA-IO	F	66	Dry and sensitive	-
9	PO-GE	F	63	Dry and sensitive	-
10	RA-NI	F	63	Normal and sensitive	-
11	CI-TA	F	62	Normal and non-sensitive	-

Individual values of the dermatological examination
D1

Treated site ID-16/11046 : right elbow bend					
Inclusion No	**T 0**			**T 45 minutes**	
	Before stripping	**After stripping**	**Unstripped**	**Stripped**	**Unstripped**
1	-	Erythema 0.5	-	-	-
2	Dryness 1	Dryness 1	Dryness 1	Dryness 0.5	Dryness 0.5
3	-	Erythema 0.5	-	-	-
4	-	Erythema 0.5	-	-	-
5	-	Erythema 1	-	Erythema 0.5	-
6	Dryness 0.5	Erythema 1 Dryness 0.5	Dryness 0.5	Dryness 0.5	Dryness 0.5
7	-	Erythema 1	-	-	-
8	Dryness 0.5	Erythema 1 Dryness 0.5	Dryness 0.5	Erythema 0.5	-
9	Dryness 1	Erythema 0.5 Dryness 1	Dryness 1	Dryness 0.5	Dryness 0.5
10	-	Erythema 0.5	-	Erythema 0.5	-
11	-	Erythema 0.5	-	-	-
Sum of reactions	**0**	**7**	**0**	**1.5**	**0**

Control site : left elbow bend					
Inclusion No	**T 0**			**T 45 minutes**	
	Before stripping	**After stripping**	**Unstripped**	**Stripped**	**Unstripped**
1	-	Erythema 1	-	-	-
2	Dryness 1	Dryness 1	Dryness 1	Dryness 1	Dryness 1
3	-	Erythema 0.5	-	-	-
4	-	Erythema 0.5	-	-	-
5	-	Erythema 0.5	-	-	-
6	Dryness 0.5	Erythema 0.5 Dryness 0.5	Dryness 0.5	Dryness 0.5	Dryness 0.5
7	-	Erythema 1	-	-	-
8	Dryness 0.5	Erythema 1 Dryness 0.5	Dryness 0.5	Dryness 0.5	Dryness 0.5
9	Dryness 1	Erythema 0.5 Dryness 1	Dryness 1	Dryness 1	Dryness 1
10	-	Erythema 0.5	-	Erythema 0.5	-
11	-	Erythema 0.5	-	-	-
Sum of reactions	**0**	**6.5**	**0**	**0.5**	**0**

Rating: 0.5 = very slight; 1 = slight; 2 = moderate; 3 = strong

Individual values of the dermatological examination
D2

Treated site ID-16/11046 : right elbow bend					
Inclusion No	**T 0**			**T 45 minutes**	
	Before stripping	**After stripping**	**Unstripped**	**Stripped**	**Unstripped**
1	-	Erythema 0.5	-	-	-
2	Dryness 1	Erythema 0.5 Dryness 1	Dryness 1	Dryness 0.5	Dryness 0.5
3	-	Erythema 0.5	-	-	-
4	-	Erythema 0.5	-	-	-
5	-	Erythema 0.5	-	-	-
6	Dryness 0.5	Erythema 0.5 Dryness 0.5	Dryness 0.5	-	-
7	-	Erythema 1	-	-	-
8	Dryness 0.5	Erythema 0.5 Dryness 0.5	Dryness 0.5	-	-
9	Erythema 0.5 Dryness 1	Erythema 1 Dryness 1	Erythema 0.5 Dryness 1	Dryness 0.5	Dryness 0.5
10	-	Erythema 0.5	-	-	-
11	-	Erythema 0.5	-	-	-
Sum of reactions	**0.5**	**6.5**	**0.5**	**0**	**0**

Control site : left elbow bend					
Inclusion No	**T 0**			**T 45 minutes**	
	Before stripping	**After stripping**	**Unstripped**	**Stripped**	**Unstripped**
1	-	Erythema 0.5	-	-	-
2	Dryness 1	Erythema 0.5 Dryness 1	Dryness 1	Dryness 1	Dryness 1
3	-	-	-	-	-
4	-	Erythema 0.5	-	-	-
5	-	Erythema 0.5	-	-	-
6	Dryness 0.5	Erythema 0.5 Dryness 0.5	Dryness 0.5	Dryness 0.5	Dryness 0.5
7	-	Erythema 0.5	-	-	-
8	Dryness 0.5	Erythema 0.5 Dryness 0.5	Dryness 0.5	Dryness 0.5	Dryness 0.5
9	Erythema 0.5 Dryness 1	Erythema 1 Dryness 1	Erythema 0.5 Dryness 1	Dryness 1	Dryness 1
10	-	Erythema 1	-	-	-
11	-	Erythema 1	-	-	-
Sum of reactions	**0.5**	**6.5**	**0.5**	**0**	**0**

Rating: 0.5 = very slight; 1 = slight; 2 = moderate; 3 = strong

Individual values of the dermatological examination
D3

Treated site ID-16/11046 : right elbow bend					
Inclusion No	**T 0**			**T 45 minutes**	
	Before stripping	**After stripping**	**Unstripped**	**Stripped**	**Unstripped**
1	-	Erythema 1	-	-	-
2	Dryness 0.5	Erythema 0.5 Dryness 0.5	Dryness 0.5	Dryness 0.5	Dryness 0.5
3	-	Erythema 0.5	-	-	-
4	-	Erythema 0.5	-	-	-
5	-	Erythema 0.5	-	-	-
6	Dryness 0.5	Erythema 0.5 Dryness 0.5	Dryness 0.5	-	-
7	-	Erythema 0.5	-	-	-
8	Dryness 0.5	Erythema 1 Dryness 0.5	Dryness 0.5	-	-
9	Dryness 1	Erythema 0.5 Dryness 1	Dryness 1	Dryness 0.5	Dryness 0.5
10	Erythema 0.5	Erythema 1	Erythema 0.5	-	-
11	-	Erythema 1	-	-	-
Sum of reactions	**0.5**	**7.5**	**0.5**	**0**	**0**

Control site : left elbow bend					
Inclusion No	**T 0**			**T 45 minutes**	
	Before stripping	**After stripping**	**Unstripped**	**Stripped**	**Unstripped**
1	-	Erythema 0.5	-	-	-
2	Dryness 0.5	Erythema 0.5 Dryness 1	Dryness 1	Dryness 1	Dryness 1
3	-	Erythema 0.5	-	-	-
4	-	Erythema 0.5	-	-	-
5	-	Erythema 0.5	-	-	-
6	Dryness 0.5	Erythema 0.5 Dryness 0.5	Dryness 0.5	Dryness 0.5	Dryness 0.5
7	-	Erythema 0.5	-	-	-
8	Dryness 0.5	Erythema 0.5 Dryness 0.5	Dryness 0.5	Dryness 0.5	Dryness 0.5
9	Dryness 1	Erythema 0.5 Dryness 1	Dryness 1	Dryness 1	Dryness 1
10	Erythema 0.5	Erythema 1	Erythema 0.5	-	-
11	-	Erythema 1	-	-	-
Sum of reactions	**0.5**	**6.5**	**0.5**	**0**	**0**

Rating: 0.5 = very slight; 1 = slight; 2 = moderate; 3 = strong

Individual values of the dermatological examination
D4

Treated site ID-16/11046 : right elbow bend					
Inclusion No	**T 0**			**T 45 minutes**	
	Before stripping	**After stripping**	**Unstripped**	**Stripped**	**Unstripped**
1	-	Erythema 0.5	-	-	-
2	Dryness 0.5	Erythema 0.5 Dryness 0.5	Dryness 0.5	-	-
3	-	Erythema 0.5	-	-	-
4	-	Erythema 0.5	-	-	-
5	-	Erythema 0.5	-	Erythema 0.5	-
6	-	Erythema 1	-	-	-
7	-	Erythema 1	-	-	-
8	Dryness 0.5	Erythema 1 Dryness 0.5	Dryness 0.5	-	-
9	Erythema 0.5 Dryness 0.5	Erythema 1 Dryness 0.5	Erythema 0.5 Dryness 0.5	-	-
10	-	Erythema 0.5	-	-	-
11	-	Erythema 1	-	-	-
Sum of reactions	**0.5**	**8**	**0.5**	**0.5**	**0**

Control site : left elbow bend					
Inclusion No	**T 0**			**T 45 minutes**	
	Before stripping	**After stripping**	**Unstripped**	**Stripped**	**Unstripped**
1	-	Erythema 1	-	-	-
2	Dryness 1	Erythema 0.5 Dryness 1	Dryness 1	Dryness 1	Dryness 1
3	-	-	-	-	-
4	-	Erythema 0.5	-	-	-
5	-	Erythema 1	-	-	-
6	Dryness 0.5	Erythema 0.5 Dryness 0.5	Dryness 0.5	-	-
7	-	Erythema 0.5	-	-	-
8	Dryness 0.5	Erythema 0.5 Dryness 0.5	Dryness 0.5	Dryness 0.5	Dryness 0.5
9	Erythema 0.5 Dryness 1	Erythema 1 Dryness 1	Erythema 0.5 Dryness 1	Dryness 1	Dryness 1
10	-	Erythema 0.5	-	-	-
11	-	Erythema 1	-	-	-
Sum of reactions	**0.5**	**7**	**0.5**	**0**	**0**

Rating: 0.5 = very slight; 1 = slight; 2 = moderate; 3 = strong

Individual values of the dermatological examination
D5

Treated site ID-16/11046 : right elbow bend					
Inclusion No	**T 0**			**T 45 minutes**	
	Before stripping	**After stripping**	**Unstripped**	**Stripped**	**Unstripped**
1	-	Erythema 1	-	-	-
2	Dryness 0.5	Erythema 0.5 Dryness 0.5	Dryness 0.5	-	-
3	-	Erythema 0.5	-	-	-
4	-	Erythema 0.5	-	-	-
5	-	Erythema 0.5	-	-	-
6	-	Erythema 0.5	-	-	-
7	-	Erythema 2	-	Erythema 0.5	-
8	-	Erythema 0.5	-	-	-
9	Dryness 0.5	Erythema 1 Dryness 0.5	Dryness 0.5	-	-
10	-	Erythema 1	-	-	-
11	-	Erythema 1	-	-	-
Sum of reactions	**0**	**9**	**0**	**0.5**	**0**

Control site : left elbow bend					
Inclusion No	**T 0**			**T 45 minutes**	
	Before stripping	**After stripping**	**Unstripped**	**Stripped**	**Unstripped**
1	-	Erythema 0.5	-	-	-
2	Dryness 1	Erythema 0.5 Dryness 1	Dryness 1	Dryness 1	Dryness 1
3	-	Erythema 0.5	-	-	-
4	-	-	-	-	-
5	Erythema 0.5	Erythema 1	Erythema 0.5	-	-
6	Erythema 0.5 Dryness 0.5	Dryness 0.5	Dryness 0.5	Dryness 0.5	Dryness 0.5
7	-	Erythema 2	-	-	-
8	Dryness 0.5	Erythema 0.5 Dryness 0.5	Dryness 0.5	Dryness 0.5	Dryness 0.5
9	Dryness 1	Erythema 0.5 Dryness 1	Dryness 1	Dryness 1	Dryness 1
10	-	Erythema 1	-	-	-
11	-	Erythema 1	-	-	-
Sum of reactions	**1**	**7.5**	**0.5**	**0**	**0**

Rating: 0.5 = very slight; 1 = slight; 2 = moderate; 3 = strong

ANNEX 2

Abstract of the study report

RESUME DU RAPPORT D'ETUDE

EVALUATION DE LA COMPATIBILITE CUTANEE D'UN PRODUIT COSMETIQUE APRES APPLICATIONS REPETEES SUR LA ZONE DU PLI DU COUDE PENDANT 5 JOURS CONSECUTIFS SUR PEAU STRIPPEE ET NON STRIPPEE SOUS CONTROLE DERMATOLOGIQUE - TEST OUVERT PAR APPLICATIONS REPETEES (Rapport clinique sur 11 volontaires adultes)

- **Produit étudié** : GEL NETTOYANT DOUX EASY TATOO
  GEL NETTOYANT DOUX EASY PIERCING –
  REF : CTG152136/0/02 CTG152138/0/02
  Code ID-16/11046

- **Promoteur** : FAREVACARE

- **Objectif de l'étude** : Evaluer la compatibilité cutanée d'un produit cosmétique appliqué 1 fois par jour sur le pli du coude sur site strippé et non strippé pendant 5 jours au centre d'étude (de J1 à J5).

- **Investigateur** : Docteur Ioana Silvia SIMIAN, Dermatologue

- **Lieu de l'étude** : CTI, Street Iuliu Teodori, Number (no.) 1, Sector 5, 010221 BUCHAREST, Romania

- **Dates de l'étude** : Du 30/01/2017 au 03/02/2017

- **Méthodologie** : Etude monocentrique, ouverte, comparative entre sites traité et témoin.

  - ✓ ***Durée, posologie et conditions d'application :*** Application quotidienne de 0,07 ml du produit sur le pli du coude (zone de 35 cm²). Chaque application est effectuée au centre d'étude sur les sites strippé et non strippé ; le volontaire pliera ensuite ses avant-bras sur ses bras pendant 15 minutes.

  - ✓ ***Méthodes d'évaluation :***
    La cotation clinique est effectuée 45 minutes après application du produit au centre et prend en compte l'érythème, l'œdème, les papules, les vésicules et les bulles. Selon leur intensité, la cotation s'échelonne de 0 à 3. La somme des scores, divisée par le nombre de sujets et le nombre d'applications, définit l'indice d'irritation moyen (I.I.M) qui permet de classer arbitrairement le produit en « non irritant », « légèrement irritant », « moyennement irritant » et « très irritant ».

- **Population étudiée** : 11 volontaires adultes (10 femmes et 1 hommes), d'âge moyen de 53 ans, compris entre 25 et 66 ans et ayant tout type de peau au niveau du corps (pli du coude), ont été inclus.

- **Résultats** : L'indice d'irritation moyen du produit est égal à 0,05 sur site strippé à T45min (témoin = 0,01).
  L'indice d'irritation moyen du produit est égal à 0 sur site non strippé à T45min (témoin = 0).

❖ **Conclusion** :

Dans les conditions de l'étude, le produit GEL NETTOYANT DOUX EASY TATOO GEL NETTOYANT DOUX EASY PIERCING - REF : CTG152136/0/02 CTG152138/0/02, appliqué 1 fois par jour pendant 5 jours consécutifs sur le pli du coude de 11 volontaires adultes (10 femmes et 1 homme), peut être considéré comme non irritant.

ABSTRACT OF THE STUDY REPORT

ASSESSMENT OF CUTANEOUS COMPATIBILITY OF A COSMETIC PRODUCT AFTER REPEATED APPLICATIONS ON THE AREA OF THE ELBOW BEND FOR 5 CONSECUTIVE DAYS ON STRIPPED SKIN AND UNSTRIPPED SKIN UNDER DERMATOLOGICAL CONTROL - REPEATED OPEN APPLICATION TEST
(Clinical report on 11 adult volunteers)

- **Investigated product** : GEL NETTOYANT DOUX EASY TATOO
  GEL NETTOYANT DOUX EASY PIERCING –
  REF : CTG152136/0/02 CTG152138/0/02
  Code ID-16/11046

- **Sponsor** : FAREVACARE

- **Purpose of the study** : Evaluate level of overall cutaneous compatibility after a 5 day repeated application period on the elbow bend, once a day, on stripped skin and unstripped skin, once at the centre (from D1 to D5).

- **Investigator** : Doctor Ioana Silvia SIMIAN, Dermatologist

- **Site of the investigation** : CTI, Street Iuliu Teodori, Number (no.) 1, Sector 5, 010221 BUCHAREST, Romania

- **Period of investigation** : From 30/01/2017 to 03/02/2017

- **Methodology** : Monocentric open comparative study between control and treated site.

  - ✓ ***Duration, dosage and application conditions****:* Daily application of 0.07 ml of the product on the elbow bend (area of 35 cm²). Every application is made in the centre of study on a stripping site and a no stripping site; the volunteer will fold then his forearms on the arms during 15 minutes.

  - ✓ ***Assessment methods:***
    The clinical quotation is made 45 minutes after the application of the product at the centre and takes in account the erythema, the oedema, the papules, the vesicles and the blisters. According to their intensity, the quotation is spread out from 0 to 3. The total sum of the scores, divided by the number of volunteers and by the number of applications, define the mean irritation index (M.I.I.) which allows to classify arbitrarily the product into "non irritant", "slightly irritant", "moderately irritant" and "very irritant".

- **Studied population** : 11 adult volunteers (10 women and 1 man), with an average age of 53 years, between 25 and 66 years and with all type of body skin (elbow bend), were included.

- **Results** : The mean irritation index of the product is equal to 0.05 on stripping site at T45min (control site = 0.01).
  The mean irritation index of the product is equal to 0 on no stripping site at T45min (control site = 0).

❖ **Conclusion** :

Under the conditions of the study, the product GEL NETTOYANT DOUX EASY TATOO GEL NETTOYANT DOUX EASY PIERCING - REF : CTG152136/0/02 CTG152138/0/02 can be considered as <u>non irritant</u> after a 5 day repeated application period on the elbow bend, once a day, of 11 adult volunteers (10 women and 1 man).

ANNEX 3

Standard protocol 1.04.D.STR_5J

Protocol: n° 1.04.D.STR_5J – 16-03

Assessment of cutaneous compatibility of a cosmetic product after repeated applications on the area of the elbow bend for 5 consecutive days on stripped skin and unstripped skin under dermatological control - repeated open application test

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- **Editor:**
  Melissa MIGNARD, Dermatologist

- **Present protocol dated as of:**
  January 4th 2016

CONTENTS

1. PURPOSE OF THE STUDY

The purpose of the study will be to assess the compatibility level of the tested product under exaggerated use conditions as compared to normal use conditions on the forearm (near elbow bend where the skin is thinner), stripped area (successive application of 5 strips of Sellotape) and non stripped skin after 5 days of repeated applications, under dermatological control. The applications will be carried out at the centre from D1 to D5 and at home of the volunteer (following the request of the sponsor) from D1 to D4.

The stripping allows to lead a slight cutaneous reaction (mechanical action on the folded layer) to get closer to the sensitive skin, in particular to the sensitive skin of the very young child or to the external genital area.

2. INVESTIGATED POPULATION

2.1. Number of subjects

n volunteers, men or/ and women will be included (10% more will be recruited in order to have the requested number of completed subjects at the end of the study).

2.2. Characteristics of the investigated population

Healthy volunteers, from the general IDEA Clinic panel of the volunteers, or, if applicable, of its sub-contractor. Every volunteer to be admitted into the panel must be subject of a medical validation by a medical doctor of the centre and undergo a clinical examination with a medical history in order to confirm that he/she is a healthy volunteer and prove that he/she benefits from social security medical coverage and is of age. From this panel, volunteers who met the inclusion criteria will be invited then definitely admitted into the study at the end of the initial examination. Participation in the study is voluntary, whereby the nature of the trials and their consequences are fully explained to the volunteers.

2.3. Criteria for inclusion

The following criteria should be fulfilled for including a volunteer in the trial:

- Healthy volunteers aged from 18 years to 70 years;
- Volunteers with sensitive skin on forearms (according to the class of the product);
- Female or male sex;
- Volunteers with a phototype between I and III;
- Volunteers with all type of skin on forearms;
- Volunteers with hairsless forearms;
- Normality of the previous medical examination;
- Free of any dermatological lesion on the site under investigation;
- Free of any past allergy to cosmetic or domestic products, Sellotape and atopy;
- Volunteers having signed a free clarified express written agreement giving their consent;
- Women using a contraceptive method to avoid to be pregnant during the test;
- Volunteer able to understand the trial's requirements;
- **Other criteria to be defined with the Sponsor.**

2.4. Criteria for non inclusion

Volunteers fulfilling the following criteria will not be included:

- Volunteers with intolerant or hypersensitive or non healthy skin on forearms;
- Volunteers who had applied a skin care cosmetic product or a pharmaceutical product within the 48 hours preceding the beginning of the trial, on the cutaneous areas under investigation;
- Evolutive cutaneous pathology;
- Under antihistaminic treatment and/or any other treatment which might interfere with cutaneous metabolism;
- Pregnant or breast feeding women;
- Subject in an exclusion period between two trials.

2.5. Exclusion from the study

2.5.1. Criteria

A volunteer may be excluded from the study for the following reasons:

- In case of an emergency of a non inclusion criteria during the study;
- On his/ her own demand;
- On a decision from the investigator, especially for non-compliance:
  - In case of isolated non-compliance with the protocol and if the deviation is considered as minor, the investigator or clinical assistant under the responsibility of the investigator will remind the volunteer of the importance to respect the protocol and the volunteer will be considered as compliant;
  - In case of repeated non-compliance with the protocol, even if the deviation is considered as minimal, or in case of major protocol deviations, the volunteer will be declared non-compliant. He /she will then be excluded for non-compliance.
- In case of a serious adverse event;
- In case of a serious disease during the study;
- For administrative reasons (e.g.: impossibility of pursuing the investigation, withdrawal).

In any case, the sponsor shall be informed of the exclusion from the investigation and on its reason. The latter shall be clearly described in the study report. Subjects excluded from the study are not replaced.
In the case of subjects “lost to follow-up”, everything should be done in order to contact the subject and to find out the reason for her/his withdrawal.

2.5.2. Procedure to be followed

When it has been decided to include 15% of additional volunteers in comparison to the number of exploitable results expected, no condition of replacement is planned in the event of volunteers dropping out or losing contact with them, for reasons not related to the study.
In case of intolerance, the volunteer will be taken into account in the tolerance analysis.

3. ASSESSMENT CRITERIA

The skin compatibility of the product will be assessed on D1, D2, D3, D4 and D5 by the investigator on T0, immediately after stripping on the stripped site then 45 minutes after application of the product on stripped sites and not stripped. It will be carried out before any application form D1 to D4 if there is an application at home, the previous evening.

The clinical quotation of skin reactions will take into account the erythema, the oedema, the papules, the vesicles and the blisters; it will be performed according to the following scale:

- 0 : absence
- 0.5 : very slight
- 1 : slight
- 2 : moderate
- 3 : strong

All other observed dermatological reaction (eg, desquamation, dryness, hypo- or hyperpigmentation) will be appropriately recorded on the data sheet and described as very slight, slight, moderate or strong.

If an erythema appears and its grading is equal or is greater than 2, it must be confirmed by a dermatologist (the investigator must be the same throughout the study), he/she will take a photograph and note in the CRF:

- the localization (treated site or other)
- when the reaction occurs
- the duration of the reaction (5-10, 10-15, 15-30, more than 30 minutes)
- the evolution (quickly regressive or not)

At the end of the study, a mean irritation index (M.I.I.) will be calculated at two reading times according to the following formula:

$$\frac{\text{Sum of the skin reactions}}{\text{Number of analysed subjects X number of applications}}$$

The M.I.I. obtained will allow to classify arbitrarily the product using the scale in the table below:

M.I.I.	**Classification of the irritation degree**
$\leq$ 0.20	Non irritant
From 0.20 (non included) to 0.50	Slightly irritant
From 0.50 (non included) to 2	Moderately irritant
From 2 (non included) to 3	Very irritant

The M.I.I. will be also calculated on the control untreated sites; it will be compared with the M.I.I. obtained with the tested product. Besides, the subjective felt signs (tingling sensation, itching, burning sensation …) will be reported in the square "others" of the observation book, according to a scale going from 0 (no sensation) to 3 (important sensation).

4. MATERIAL

4.1. Product to be tested

Not applicable (standard protocol).

4.2. Modes of application/use

Five applications of the product or 2 µl / cm² of the product, that is to say 0.07 ml of the product will be applied daily on an area of 35 cm² (5X7 cm) on the right elbow bend, following modalities of use defined by the Sponsor. If the product is a wipe, five applications were made. After applying the product, the volunteer will fold his forearms on the arms for 15 minutes. Any observed skin reactions will be reported in the log book by the investigator and he/she will gather impressions on the product's skin tolerance 30 minutes after extending the arms. If there is an application at home, a syringe with 0.07 ml of the product or a wipe will be given to the volunteer from D1 to D4, without bending the arms.

5. METHODOLOGY FOR THE STUDY AND PROCEDURE

5.1. Procedure for selecting subjects

5.1.1. Review of the selection procedures

Selected subjects who meet the criteria defined in paragraphs 2.3 and 2.4 (criteria for inclusion/criteria for non inclusion), shall be considered as fit for the trial.

5.1.2. Clarified consent

An information note will be handed to each volunteer during the initial examination (V1) and the evaluator will explain to them how the trial is conducted. He will ask them to notify any adverse event, any beginning of pregnancy (for the women) and any drug treatment occurring during the test.
The evaluator will collect the written, informed, free and express consent of the volunteer by means of the prepared form for this purpose, before any application of the product.
The evaluator will keep one consent intended to be archived in the study file and another one will be given to the volunteer.

5.1.3. Confidentiality of source documents of the study

The forms for consent to participate in the study will be retained in the file. At all events, the people to whom this information is communicated should consider it to be confidential.

5.1.4. Associated treatments

Any drug or other treatment administered during the investigation should be recorded in the observation book with reference to the trade name, dosage, duration of the treatment and its indication.

5.1.5. Authorized drugs

Authorized drugs are noted on the internal guidebook in force.

5.1.6. Unauthorized drugs

Anti-inflammatories, corticoids, antihistaminics and any treatment reducing or inhibiting inflammatory or allergic reactions are strictly forbidden. Unauthorized drugs are noted on the internal guidebook in force.

5.1.7. Specific associated measures

For the whole period of the study, each volunteer is required:

- To avoid being exposed to U.V. radiation (whether natural or artificial);
- Not to change his/her habits relative to personal hygiene and use of cosmetics;
- Not to use any other cosmetic product of the same range as the one being tested;
- Nothing is to be applied on the control and treated forearm;
- To avoid beauty treatment in beauty salon.

5.2. Conducting the investigation

5.2.1. Introduction

Assessments should be carried out by the same person throughout the clinical investigation when this is possible.

If this is not possible, the assessments should be jointly carried out during at least one visit (the volunteer shall be examined by both persons and the results will be discussed together).

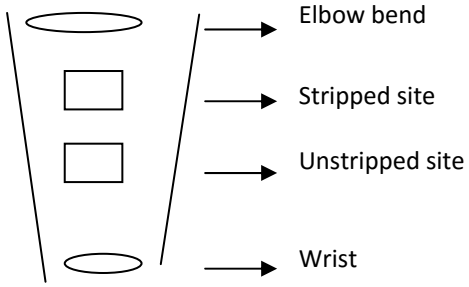
5.2.2. Procedure to be followed at each visit

Each application of the product will be performed in the centre by a clinical assistant under the responsibility of the investigator on unstripped and stripped skin. The product will be apply at home on the same sites.

Visit on D1

- Inform the volunteer on how the investigation is conducted.
- Collect the volunteer's clarified written agreement giving his consent.
- Enter in the log book, demographic data and those from the clinical examination of the cutaneous area which will receive the product as well as possible treatments taken by the volunteer.
- Check compliance with inclusion and non inclusion criteria. If the volunteer qualifies according to these criteria, she is eligible for the study and is included in it.
- Successively assign the volunteer's number in an ascending order relatively to her arrival into the study.

Step 1: determination of 4 sites on an area of about 35cm² (5 x 7 cm), (2 sites on each forearm) located on the anterior side of the elbow bend according to the following diagram:



Step 2: on sites to strip, successive application then removal of 5 strips of Sellotape to lead a slight cutaneous reaction (mechanical action on the folded layer). Reading the cutaneous reactions immediately after the stripping.

Step 3: Application of the tested product according to the modes of application described in § 4.2 on the area near to the right elbow bend (stripped and unstripped sites); the left controlateral area is the control site (stripped and unstripped sites).

Step 4: Flexion of the forearms on arms for 15 minutes.

Step 5: Extension of the forearms for 30 minutes.

Step 6: Clinic examination and collection of the impressions on skin tolerance (45 minutes after application).

Step 7: Delivery of the quantity to apply for the application at home if needed.

Visits from D2 to D5

Before any other application of the product, clinical examination of the areas, treated and control site reading, collection of the impressions on the product's skin tolerance will be performed then the study will be conducted according to step 2 to 6. If there is an application at home, this application will be verified and the volunteer will get the necessary quantity for the next application.

5.3. Conducting the visits and the examinations

The clinical examination of the treated and control sites took place before any application and 45 minutes after application at the centre of study from D1 to D5.

Site	D1		D2, D3, D4 and D5	
	Before application of the product	**45 minutes after application of the product**	**Before 2nd, 3rd, 4th and 5th application**	**45 minutes after 2nd, 3rd, 4th and 5th application**
Elbow bend	X	X	X	X

Types of control: clinical examination of the treated and control sites (stripped and unstripped) receiving the product.

5.4. Ceasing the investigation

The sponsor or the investigator reserves the right of interrupting the investigation at any time after appropriate notification.

5.5. Period of investigation

X days.

6. RECORDING DATA

All the information will be entered in the CRF which could be digital via our Camelia data base. Necessary corrections should be dated and initialled by the investigator or the clinical assistant under the investigator responsibility.
The first writing should remain legible.

7. UNDESIRABLE EVENT

7.1. Definition

For the whole period of investigation, all undesirable events will be traced and recorded in the log book section provided for this purpose. The seriousness or lack of seriousness of the event, its severity level, the date on which it occurs, its duration, the actions taken and the causal relation with the trial product will also be recorded in the log book.

7.1.1. Undesirable event

An undesirable event is defined as any unfortunate medical circumstance experienced by a person during the course of the trial, whether it is considered as being related to the investigated product or not.

7.1.2. Serious undesirable event

A serious adverse event is an adverse event which results in persistent or significant disability/incapacity, which results in any hospitalisation, is life-threatening, results in death or is a congenital anomaly or birth defect.
Any adverse event that does not correspond to the situations previously mentioned but appearing to have a serious aspect will be considered as serious by the Investigator and will be notified as a SAE.

7.1.3. Severity

To assess the severity level of an undesirable event, the investigator shall resort to the following indications:

- Slight: visible by the subject, but it does not require any treatment and it does not interfere with the daily activities of the subject
- Moderate: awkward, it may require treatment, but it does not interfere with the daily activities of the subject
- Severe: intolerable, requires treatment may or may not interfere with the daily activities of the subject

7.1.4. Relationship with the investigated product

The investigator shall attempt to establish a causal relation between the occurrence of an adverse event and the product being tested with the help of the following indications:

- Null: a simultaneous illness, a simultaneous treatment or any other known cause are clearly responsible for the adverse effect.
- Doubtful: this relationship exists when the adverse effect follows a not very reasonable chronological sequence from the moment the product is administered and /or the type of observed reaction is not very compatible with the range of product, without repetition of the same reaction after re-applying the product.
- Possible: this relationship exists when the adverse effect follows a reasonable chronological sequence from the moment the product is administered and /or the type of observed reaction is compatible with the range of product, without repetition of the same reaction after re-applying the product.
- Likely: this relationship exists when the adverse effect follows a reasonable chronological sequence from the moment the product is administered and /or the type of observed reaction is compatible with the range of product, without a doubtful reaction after re-applying the product.
- Very likely: this relationship exists when the adverse effect follows a reasonable chronological sequence from the moment the product is administrated and when the type of observed reaction is compatible with the range of product, with repetition of the same reaction after re-applying the product.

7.2. What to do in the case of an undesirable event

Suitable measures should be taken for treating undesirable events which have occurred during the investigation. Any subject having undergone an undesirable event should be monitored both clinically and biologically until his/her parameters return to their normal values.
All undesirable events as well as their outcome should be reported to the sponsor and recorded in the form provided for this purpose in the log book.

All adverse events as well as their outcome should be quickly reported by the investigator to the study monitor (within a 24 hour period for the SAE) by telephone or mail and recorded in the form provided for this purpose in the CRF. The investigator will give all complementary information to the Sponsor.

Case of a pregnancy:

- if a pregnancy is suspected during the inclusion: the volunteer will not be included in the study;
- if a pregnancy is suspected during the test, this one must be stopped until the results of the biological pregnancy test. If the pregnancy is confirmed, then the pregnancy is notified to the Sponsor on the SAE form. The volunteer is definitively excluded from the study. The Investigator must follow the volunteer until the end of her pregnancy or of her termination and must notify the outcome to the Sponsor.

8. METHODS FOR STATISTICAL ANALYSES

The analysis of subjective skin compatibility by the volunteer will be determined by descriptive statistics.
A description of individual assessments is shown for each visit.
The mean irritation index as calculated in §3 will be taken into account for the analysis of skin compatibility.
The results of M.I.I. on the stripped skin will be compared to those obtained on the unstripped skin.

9. PROCEDURE IN THE EVENT OF DIVERGENCE FROM THE PROTOCOL

For all divergence from the protocol considered “noteworthy”, the procedure to respect is as follows:

- each volunteer mistakenly included will not be included in the analysis;
- If a criterion for exclusion manifests itself during the study, the excluded volunteer will not be included in the analysis;
- If the procedures of the study are not respected:
  - If the non-respect has an impact on the validity of the interpretation of the results, the volunteer will not be included in the analysis and will be excluded ;
  - If the non-respect is minor in nature, the volunteer will be included in the analysis.

In any event, protocol deviation is to be noted in the study report and the applied procedure justified.

In an emergency, the investigator shall bring in any medical treatment or any procedure which may seem appropriate. These treatments and procedures shall be reported as quickly as possible to the study supervisor.

The data from all excluded volunteers will not be taken into account.

The data from the volunteers who withdrew during the study (“lost to follow up” or withdrawal for personal reasons) will not be taken into account.

10. PROTOCOL AMENDMENT

Except in case of emergency, no amendment or deviation to the protocol will be accepted without the study Sponsor authorisation.
Every modification of the protocol will be validated by a protocol amendment.

11. END OF STUDY RULES

The study will end when all the study volunteers will have attended the end of study visit (except for the “lost to follow up”).

12. GOOD CLINICAL PRACTICE

The study will be carried out in accordance with the European directives Good Clinical Practice (EU directives, July1990).

13. ETHICAL AND LEGAL CONSIDERATIONS

13.1. Regulations

This study, without direct therapeutic end for the volunteer, will be produced in accordance with the most recent recommendations of the Worldwide Medical Association (1964 Helsinki Declaration, recently amended in Fortaleza, Brazil, 2013). Not entering within the area of application of French law n° 88-1138 of December 20th 1988 modified by laws n° 90-86 of January 23rd 1990 and n° 94-630 of July 25th 1994, as indicated in the "guide des textes législatifs et réglementaires" (B.O.M.S. n°91/13b), relating to the protection of persons volunteering for biomedical research, no information will be communicated to the National file of persons volunteering for biomedical research without direct individual benefit and the opinion of the Consulting Committee was not sought. On the other hand, the spirit of Decree 90-872 of September 27th 1990 concerning application of this law will be respected.

13.2. Keeping the investigation's documentation

The investigator shall keep documents relating to the trial (final report, CRF, data) in an archive room at IDEA Clinic or of its sub-contractor for 2 years after the archiving year. Study documents of the previous years will be archived by an external company.
The period of keeping the documentation depends on the nature of the studied product, that is to say 10 years for the studies of cosmetic products.
After this period, the data will be destroyed, unless otherwise explicitly demanded by the promoter asking us to return them.

13.3. Insurance

The study will be covered by the insurance contract underwritten by the Sponsor, contract of civil responsibility covering trials on healthy volunteers.
IDEA TESTS Group took out insurance guaranteeing civil liability with respect to the volunteers.
Name of the Company: COVEA RISKS
Reference number: 128 776 308

13.4. Personnel qualification

The investigator ensures that all persons that participated in the study require competences and are authorised to exercise them.

13.5. Confidentiality

All information concerning the state of health of the panellists and the results of the clinical examinations, carried out before the study, for their recruitment, selection and admission, are subject to the rules of medical secrecy in accordance with article 378 of the Penal Code and the Code of Medical Deontology (Decree n° 95-1000, of September 6th 1995): In any case, it cannot be communicated to the Sponsor with their identity.
To ensure volunteers' anonymity, volunteers will be identified by a code with 4 letters including the first 2 letters of the surname, then the first 2 letters of their first name, and for the study, by a number corresponding to the order of their inclusion in the study.
At the end of the study, the consent and the inclusion questionnaire in which the confidential volunteer data will be recorded are archived in the study file in a sealed envelope.
The investigators and all persons called upon to participate in the trials are held to professional secrecy concerning the nature of the products studied, the trials, the persons volunteering and the final results.

13.6. Administrative formalities

Insurance for IDEA Clinic
IDEA Clinic took out insurance guaranteeing civil liability with respect to the volunteers (cf. § 13.3).

Information and free, informed and express consent
An information document will be given to each volunteer, in order to specify:

- the objective and relevance of the research;
- any expected benefits, constraints connected to the study and predictable risks, including in the event of stoppage of the study before its completion;
- the non-inclusion period, the amount of compensation, the possibility for the volunteer to verify the exactness of the data contained in his medical file and their subsequent sealed archiving;
- the possibility to stop participation in this study at any moment by informing the investigator.

This information will allow the volunteer to knowingly sign a form giving free, informed and express consent for participation.

13.7. Quality Assurance

The final report will be audited by IDEA Quality Assurance unit, which will confirm that it contains the methods for conducting the study, that the observations are wholly described and that the results represent the exact data of the study, in the spirit of Good Clinical Practice.

13.8. Signatures

IN AGREEMENT WITH THE PROTOCOL

Non applicable

Sponsor

Anne CASOLI
Doctor of medicine
IDEA Clinic manager
IDEA Clinic

Melissa MIGNARD
IDEA Clinic tolerance trial manager
Dermatologist
Editor
IDEA Clinic

Non applicable

Dr
Dermatologist
Investigator

14. BIBLIOGRAPHY

- Hannuksela M, Salo H (1986) The repeated open application test (ROAT). Contact Dermatitis 14 : 221-227

- Hannuksela A, Niinimäki A, Hannuksela M (1993) Size of the test area does not affect the result of the repeated open application test. Contact Dermatitis 28 :299-300

- Johansen JD, Bruze M, Andersen KE, Frosch PJ, Dreier B, White IR, Rastogi S, Lepoittevin JP, Menné T (1998) The repeated open application test : Suggestions for a scale of evaluation. Contact Dermatitis 39 :95-96