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Dermatest® GmbH | Postfach 2165 | 48008 Münster

ACTO GmbH

Büchnerstraße 11
D-38118 Braunschweig

Muenster, 14.01.2013

Certificate

for the Product:

Actoderm (Chargen Nr. 1108108)

Dermatological test on humans in 2013

The dermatological test performed by us on your product under the control of dermatological specialists was passed for this product with the rating of

„very good“

This product did not lead to toxic- irritative intolerance reactions in patch testing carried out in accordance with international guidelines. The preparation can therefore be declared as dermatologically tested.

Dr. med. Werner Voss
Facharzt für Dermatologie
Venerologie, Allergologie,
Phlebologie und Umweltmedizin

Dermatest GmbH
Engelstrasse 37
48143 Münster Germany
dermatest®
RESEARCH INSTITUTE FOR RELIABLE RESULTS
Taking your success personally
Fax: +49-(0)251-4 90 27 27
www.dermatest.de

Dermatest® GmbH | Engelstr. 37 | 48143 Münster | Germany

Tel.: +49 251 4882249 | Fax: +49 251 4902727
www.dermatest.de | info@dermatest.de
Geschäftsführer: Dr. med. Werner Voss
Amtsgericht Münster HRB 1348 | Münsterländische Bank Thie & Co.
BLZ 400 300 00 | Konto-Nr. 3 492 784 800 | USt-ID: DE126040147

TÜVRheinland CERT ISO 9001

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Dermatological report on human Patch Test
Test for primary skin irritation and hypersensitivity of human subjects after single application

Actoderm (Chargen Nr. 1108108)

Customer:	ACTO GmbH Büchnerstraße 11 D-38118 Braunschweig
Test Panel:	30 panellists of either sex, without visible skin diseases or known hypersensitivity
Concentration of the product:	undiluted

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PRINCIPLE AND METHODS

The objective of the study is to detect primary skin irritation potential and/or existing allergic sensitisation to the test substance.

The test substance is applied to the skin of the panellist via an occlusive patch at a suitable concentration.

The patch limits contact of the panellist's skin with the test substance to a local area and exposure is exaggerated due to the occlusive conditions. The skin is checked at 24, 48 and 72 hours.

The occlusion eases the absorption of the suspected topical allergen allowing it to penetrate the stratum corneum to the viable (effector) cells of the skin and thus presenting a local challenge to the immune system.

If the threshold level of sensitivity is reached, a positive reaction could potentially be induced.

A positive reaction to a correctly applied patch provides evidence of primary irritation to the substance tested, but is not necessarily evidence of sensitisation.

Patch testing provokes allergic skin reactions in already sensitised panellists.

PROCEDURES

Prospective panellists receive a complete explanation of study procedures. If they wish to participate and agree to the conditions of the study, panellists sign a written, informed consent and provide a medical history.

5 mg/15 µl of the undiluted test product is applied to an adhesive plaster (Curatest® F Folien-Testpflaster, Fa. Lohmann & Rauscher GmbH & Co. KG) and affixed to clinically healthy skin on the upper back. Textile products are affixed with a sample size of 0,3 cm^2 with the adhesive plaster on the upper back.

After a 24 hour exposure period, the plaster is removed and the exposed skin is dermatologically assessed and graded. The second and third assessments are performed after 48 and 72 hours respectively.

All assessments are conducted 30 minutes after removal of the test plaster.

Where a positive reaction is observed, but it is unclear whether the observed reaction is due to sensitisation or irritation, subsequent readings can be performed.

All assessments are performed under standard lighting conditions.

The panellists are instructed to keep the test sites dry.

PANELLISTS

The test panel includes 30 adult male and female panellists.
In this test panel there are always panellists with (very) dry, oily, normal and sensitiv skin.

INCLUSION CRITERIA

- Standard design: Panellists aged 18 years and above with healthy skin in the test area
- Extra designs: Special inclusion of age, gender, skin type etc. according to claim of the study

EXCLUSION CRITERIA

- Acute diseases
- Pregnancy and lactation period
- Sensitisation to ingredients of the test plaster
- Severe illnesses
- Application of pharmaceutical products and skin care products with active ingredients until 4 weeks before testing
- Intake of drugs that possibly can interfere with skin reactions (steroids, antiallergics, topical immuno modulator, etc.)
- Extremely tanned skin

RESULTS

Table 1: Results of patch-testing for the test substance
Concentration of the product: undiluted

No.	Name	Gender	Age	Diagnosis	24 h	48 h	72 h
1.	Ma. Ar.	m	35	healthy skin	-	-	-
2.	Ma. Bo.	f	55	healthy skin	-	-	-
3.	Ka. Br.	f	27	healthy skin	-	-	-
4.	Ol. Br.	m	31	healthy skin	-	-	-
5.	Ev. De.	f	44	healthy skin	-	-	-
6.	Th. De.	m	53	healthy skin	-	-	-
7.	Ga. Ge.	f	57	healthy skin	-	-	-
8.	Kl. Ge.	m	56	healthy skin	-	-	-
9.	Sv. Ho.	f	24	healthy skin	-	-	-
10.	No. Ko.	m	53	healthy skin	-	-	-
11.	Sa. Ko.	f	51	healthy skin	-	-	-
12.	Ti. Ko.	m	24	healthy skin	-	-	-
13.	Ni. Kr.	f	28	healthy skin	-	-	-
14.	Ur. Kr.	f	56	healthy skin	-	-	-
15.	Bä. La.	f	56	healthy skin	-	-	-
16.	He. La.	m	59	healthy skin	-	-	-
17.	Si. Ma.	m	19	healthy skin	-	-	-
18.	Al. Mü.	m	32	healthy skin	-	-	-
19.	De. Pe.	m	53	healthy skin	-	-	-
20.	Fr. Pe.	f	50	healthy skin	-	-	-
21.	Ja. Pe.	f	28	healthy skin	-	-	-
22.	An. Sc.	f	48	healthy skin	-	-	-
23.	Ra. Sc.	m	49	healthy skin	-	-	-
24.	Ja. Sp.	m	31	healthy skin	-	-	-
25.	Ch. Te.	f	47	healthy skin	-	-	-
26.	Ja. Te.	f	20	healthy skin	-	-	-
27.	Mi. Te.	m	47	healthy skin	-	-	-
28.	Sa. Te.	f	23	healthy skin	-	-	-
29.	Ka. Vo.	f	27	healthy skin	-	-	-
30.	Do. We.	f	31	healthy skin	-	-	-

RESULTS

Table 2: RESULTS of patch-testing for the CONTROL
Concentration of the product: blanc patch-test

No.	Name	Gender	Age	Diagnosis	24 h	48 h	72 h
1.	Ma. Ar.	m	35	healthy skin	-	-	-
2.	Ma. Bo.	f	55	healthy skin	-	-	-
3.	Ka. Br.	f	27	healthy skin	-	-	-
4.	Ol. Br.	m	31	healthy skin	-	-	-
5.	Ev. De.	f	44	healthy skin	-	-	-
6.	Th. De.	m	53	healthy skin	-	-	-
7.	Ga. Ge.	f	57	healthy skin	-	-	-
8.	Kl. Ge.	m	56	healthy skin	-	-	-
9.	Sv. Ho.	f	24	healthy skin	-	-	-
10.	No. Ko.	m	53	healthy skin	-	-	-
11.	Sa. Ko.	f	51	healthy skin	-	-	-
12.	Ti. Ko.	m	24	healthy skin	-	-	-
13.	Ni. Kr.	f	28	healthy skin	-	-	-
14.	Ur. Kr.	f	56	healthy skin	-	-	-
15.	Bä. La.	f	56	healthy skin	-	-	-
16.	He. La.	m	59	healthy skin	-	-	-
17.	Si. Ma.	m	19	healthy skin	-	-	-
18.	Al. Mü.	m	32	healthy skin	-	-	-
19.	De. Pe.	m	53	healthy skin	-	-	-
20.	Fr. Pe.	f	50	healthy skin	-	-	-
21.	Ja. Pe.	f	28	healthy skin	-	-	-
22.	An. Sc.	f	48	healthy skin	-	-	-
23.	Ra. Sc.	m	49	healthy skin	-	-	-
24.	Ja. Sp.	m	31	healthy skin	-	-	-
25.	Ch. Te.	f	47	healthy skin	-	-	-
26.	Ja. Te.	f	20	healthy skin	-	-	-
27.	Mi. Te.	m	47	healthy skin	-	-	-
28.	Sa. Te.	f	23	healthy skin	-	-	-
29.	Ka. Vo.	f	27	healthy skin	-	-	-
30.	Do. We.	f	31	healthy skin	-	-	-

INTERPRETATION CRITERIA

The assessment is based on the morphologic changes detailed in the modified guidelines of

ICDRG (Fregert S (1981/2nd edition) Manual of Contact Dermatitis. On behalf of the International Contact Dermatitis Research Group and the North American Contact Dermatitis Group, Munksgaard Publishers,Copenhagen)

Table 3. Grading of the patch test reactions

Symbol	**Morphology**	**meaning**
-	No reaction	negative
?	Only erythema, no infiltration	doubtful
+	Erythema, infiltration, possibly discrete papules	simple-positive reaction
++	Erythema, infiltration, papules, vesicles	Double- positive reaction
+++	Erythema, infiltration, papules, confluent vesicles	3-positive reaction
ir	Different changes (soap effect, vesicles, bulla, necrosis)	Irritative
nt		Not tested

GENERAL DERMATOLOGICAL INTERPRETATION CRITERIA:

The discrimination between irritation and allergy is of importance. As a general rule, a positive reaction is said to be „allergic“ if it has been graded as “+” to “+++ “ up to 72 hours or beyond.

Understanding the dynamics of the reaction may aid the assessment.

Allergic test reactions could persist("Plateau-type”) or even worsen ("Crescendo-type")on the day after the plaster has been removed). A “Decrescendo”-type (decrease of reaction after removal of plaster) on the other hand, indicates irritation.

If delayed reactions only develop 10-14 days after application, (“iatrogenic”) sensitisation should be considered.

Irritative and allergic reactions present erythema and could also cause infiltration.

Papules, vesicles and bullae could demonstrate irritation as well as allergy, whereas pustules and necrosis point to severe irritation reactions.

Both reactions could spread beyond the original application site.

Moreover the individual expression of a reaction lies within a wide range.

patch test
Actoderm (Chargen Nr. 1108108)

CONCLUSION

No evidence of any skin disorder was detected in the test area of any of the 30 panellists after conducting patch testing for 24 h, 48 h and 72 hours according to the internationally recognised guidelines of ICDRG (International Contact Dermatitis Research Group).

It can be concluded that the use of the product will not cause any unwanted skin reactions due to an irritating effect.

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Fon: +49-(0)251-4 88 22 49
Fax: +49-(0)251-4 90 27 27
www.dermatest.de

Dr. med. Werner Voss
Investigating specialist
for dermatology, allergology,
venerology, phlebology
and environmental medicine

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