STUDY REPORT

3 x 24 h Epicutaneous Patch Test

Sponsor	SpaBalancer GmbH, Halstenbek
Sponsor Contact	Tim Dörries
Study Site	proDERM Institut für Angewandte Dermatologische Forschung GmbH, Schenefeld/Hamburg
Project Manager/ Investigator	Dipl.-Biol. Christiane Röck, Schenefeld/Hamburg
proDERM Study No.	13.0330-02
Test Dates	November 04 to November 09, 2013
Report	November 15, 2013

1 Objective

The aim of this study was to assess the cumulative irritation potential of test materials to human skin as a result of repeated exposure.

2 Project Information

Project Manager/Investigator	Dipl.-Biol. Christiane Röck
Lead Technician	Dipl.-Ing. Petra Jacobs
Data Management/Statistics	Katrin Windgassen, B.A.
Report	Dr. rer. nat. Maike Keskin
Quality Assurance	Dr. rer. nat. Jutta Hofmann

3 Materials and Methods

3.1 Test Materials

The test products were provided by the Sponsor. Control materials were provided by the Study Site.

Code/proDERM	Product/Code/Sponsor	Concentration	Dilution done by:	
			proDERM	Sponsor
A	Aqua demin. (negative control)	as is	-	-
B	Sodium Dodecyl Sulfate (positive control)	0.3 % (w/w)	X	-
C	SpaBalancer	40 ml / 1000 l	-	X
D	SpaBalancer Ultrashock	40 ml / 1000 l	-	X
E	Mixture of SpaBalancer and Ultrashock	1 part C : 1 part D	X	-

Date Samples Received	October 08, 2013
Storage Conditions	Room temperature
Application Area	Back
Application Volume	25 µl
Application Mode	The test materials were applied with a Finnpipette
Patch Test System	Haye's Test Chamber®, HAL (occlusive)

3.2 Subjects

Subjects Enrolled	22
Complete Data Exclusions	None
Subjects Analyzed (Valid Cases)	22
Age	55.2 ± 16.9 years (mean ± standard deviation)
Sex	3 male (14 %) 19 female (86 %)

3.3 Methods

The study has been conducted according to the proDERM Standard Protocol-V03 (02-3x24h-PT), the Study Protocol (see Appendix F) and approximating the main principles of GCP.

3.3.1 Test Schedule

Day	**1**	**2**	**3**	**4**	**5**	**6**
Application of Test Materials	X	X	X			
Patch Removal (24 h after the last application of test materials)		X	X	X		
Visual Evaluation (By a trained evaluator, 15 min (day 4), 24 h (day 5) and 48 h (day 6) after last patch removal)				X	X	X

3.3.2 Description of Test Procedure

- The test substances and controls were applied on the back of the subjects under occlusive conditions using the above mentioned epicutaneous patch test system on day 1.
- The application was repeated on days 2 and 3 or up to the fist intense irritant reaction that would have been scored 2 or higher was noticed for the respective product.
- Visual scoring will be performed 15 minutes after removal of the last set of patches (day 4) as well as after further 24 (day 5), and 48 hours (day 6).

The assessments were performed according to the following scales:

3.3.3 Visual Evaluation

0 = No apparent cutaneous involvement

0.5 = Minimal erythema, Greater than 0, less than 1

1 = Definite erythema (may include edema)

2* = Strong erythema, may have a few papules or deep fissures, may include moderate-to-severe erythema in the cracks

3* = Severe erythema (beet redness), may have generalized papules and/or vesicles

4* = Severe erythema with edema extending clearly beyond the areas of the patch and/or bullae and/or eschar formations

***** No further product application. From the consecutive day on the maximum score was given for all further assessments for the respective product
ATTENTION: The maximum score was not given when the scoring was performed in the consecutive phase with no product application (day 4, 5 and 6).

Scores were directly entered into a PC system with an appropriate computer program.

3.4 Protocol Violations/Additional Remarks

None

4 Results

4.1 Discontinuations

During the application phase no strong irritant reactions (scored $\geq$ 2) were observed for any product. Therefore, no product discontinuations were necessary.

4.2 Irritation Scores

The results for the mean scores of all products are summarized in Table 1.

Table 1: Mean Scores (Day 4, Day 5, Day 6) and Mean Sum Score (Day 4+Day 5+Day 6) of Test Products

Product	Day 4, 15 minutes	Day 5, 24 hours	Day 6, 48 hours	Mean Score (d4 + d5 + d6)
A (Negative control)	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	**0.0 ± 0.0**
B (Positive control)	0.5 ± 0.5	0.4 ± 0.5	0.2 ± 0.3	**0.4 ± 0.4**
C	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	**0.0 ± 0.0**
D	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	**0.0 ± 0.0**
E	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	**0.0 ± 0.0**

Raw data of all valid subjects are listed in Appendix D. More information about the results is provided in Appendix A (Figures). For each test material the mean score of each evaluation time was determined as well as the mean irritation score (average of all three evaluations for each product, see Appendix B: Summary Tables). Furthermore, the scores of the three evaluations were averaged for each subject (see Appendix E: Calculated Values). A list of all subjects that have participated in this study is provided in Appendix C (List of Subjects).

5 Conclusions

The mean irritation scores induced by the tested products, **SpaBalancer** (C), **SpaBalancer Ultrashock** (D), and the **1+1 Mixture** of **SpaBalancer** and **Ultrashock** (E), all were the same as those induced by the negative control Aqua demin. (A) at all readings, with no irritation induced at all. Therefore, the skin tolerability of all tested products with respect to irritancy can be expected to be "**very good**" when used as intended.

Appendices

Appendix A:	Figures
Appendix B:	Summary Tables
Appendix C:	List of Subjects
Appendix D:	Raw Data
Appendix E:	Calculated Values
Appendix F:	Study Protocol

6 Authentication

The signatories confirm that this study was conducted, the analysis performed and the report prepared taking the principles of Good Clinical Practice (GCP) as a guide of reference for this study, and in accordance with the approved protocol(s). The principle requirements of the Declaration of Helsinki were taken into account to protect the rights, safety and well-being of subjects participating in the study. They further confirm that the reported results are a complete and accurate reflection of the clinical research data obtained in this study and based on the statistical analysis to the best of the undersigned's knowledge.

Prof. Dr. med. Klaus-Peter Wilhelm
Dermatologist
- Medical Director/Principal Investigator -

November 25, 2013
Date / Signature

Dipl. Bio-Ing. Stephan Bielfeldt
- Director Research -

November 20, 2013
Date / Signature

Dipl.-Biol. Christiane Röck
- Project Manager/Investigator -

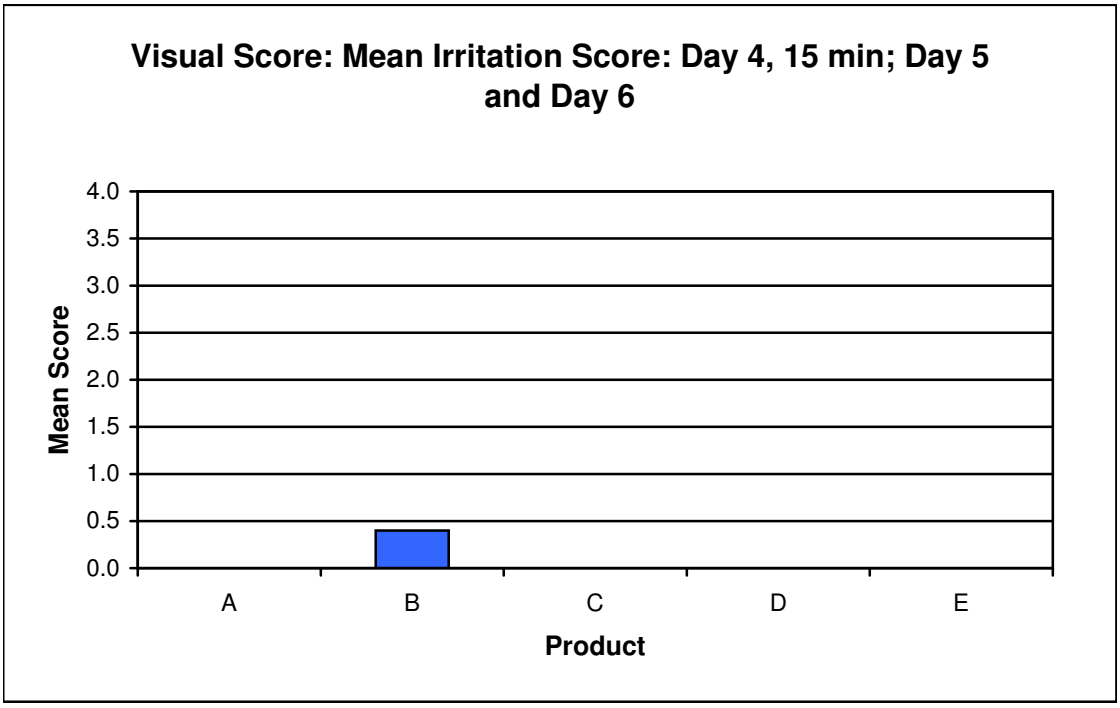
November 15, 2013 C. Röck
Date / Signature

The representative signature of the quality assurance unit signifies that quality control measures for completeness and accuracy of the clinical research data, for data analysis and for the reporting of results have been performed by responsible personnel for this study. The quality requirements for the report have been fulfilled to the best of the undersigned's knowledge. This type of study is audited by the quality assurance unit according to the audit schedule.

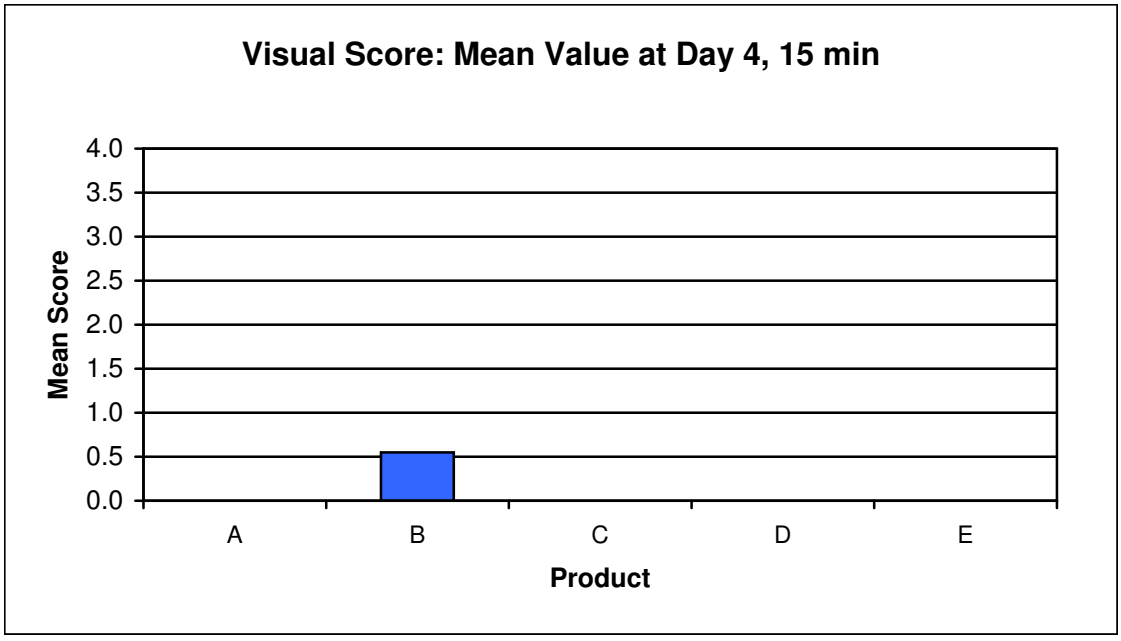
Dr. rer. nat. Jutta Hofmann
- Head of Quality Assurance/QM -

November 20, 2013
Date / Signature

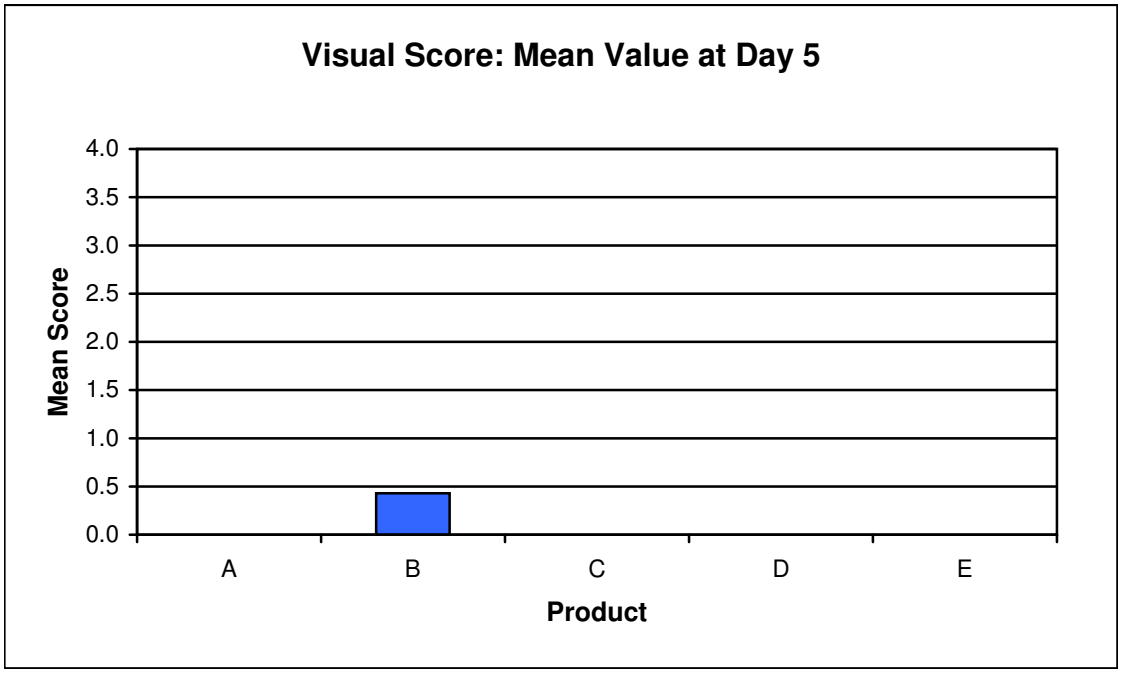
Appendix A


Visual Score: Mean Irritation Score: Day 4, 15 min; Day 5 and Day 6
Mean Score
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
A
B
C
D
E
Product

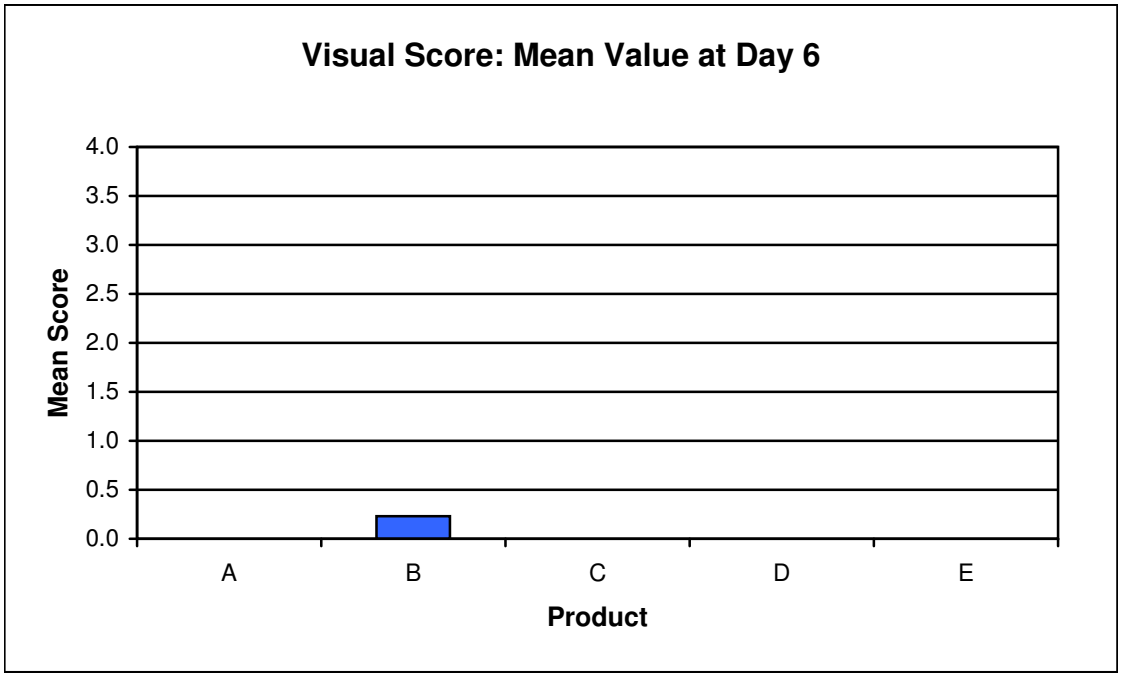
N = 22


Visual Score: Mean Value at Day 4, 15 min
Mean Score
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
A
B
C
D
E
Product

N = 22


Visual Score: Mean Value at Day 5
Mean Score
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
A
B
C
D
E
Product

N = 22


Visual Score: Mean Value at Day 6
Mean Score
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
A
B
C
D
E
Product

N = 22

Appendix B

Table: B1	Mean Values				Study-No.: 13.0330-02
Parameter: Visual Score					Parameter-ID: 171
Prod.	A	B	C	D	E
Mean/d 4, 15 '	0.0	0.5	0.0	0.0	0.0
Mean/d 5	0.0	0.4	0.0	0.0	0.0
Mean/d 6	0.0	0.2	0.0	0.0	0.0

Table: B2					Study-No.: 13.0330-02
Parameter: Visual Score: Mean Score					Formula Typ: 5
Prod.	A	B	C	D	E
Mean/d4+d5+d6	0.0	0.4	0.0	0.0	0.0

Table: B3	Day 4, 15 min				Study-No.: 13.0330-02
Number of Reactions: Visual Score					Parameter-ID: 43854
Score \ Prod.	A	B	C	D	E
0	22	7	22	22	22
0.5	0	8	0	0	0
1	0	6	0	0	0
2	0	1	0	0	0
3	0	0	0	0	0
4	0	0	0	0	0
n	22	22	22	22	22

Table: B4	Day 5				Study-No.: 13.0330-02
Number of Reactions: Visual Score					Parameter-ID: 43853
Score \ Prod.	A	B	C	D	E
0	22	8	22	22	22
0.5	0	11	0	0	0
1	0	2	0	0	0
2	0	1	0	0	0
3	0	0	0	0	0
4	0	0	0	0	0
n	22	22	22	22	22

Table: B5	Day 6				Study-No.: 13.0330-02
Number of Reactions: Visual Score					Parameter-ID: 43852
Score \ Prod.	A	B	C	D	E
0	22	13	22	22	22
0.5	0	8	0	0	0
1	0	1	0	0	0
2	0	0	0	0	0
3	0	0	0	0	0
4	0	0	0	0	0
n	22	22	22	22	22

Appendix C

Subject No.	Status	ID	Initials	Sex	Age	Atopy	Typ IV Allergies	Sensitive Skin
1	c	12663	S.B.	f	44	n	n	n
2	c	19358	J.M.	m	62	n	n	n
3	c	24076	M.S.	f	73	n	n	n
4	c	1127	U.B.	f	72	n	n	n
5	c	13872	R.O.	f	66	n	n	y
6	c	15147	R.L.	m	54	n	n	n
7	c	10591	A.H.	f	39	y	y	n
8	c	4607	B.B.	f	72	n	n	n
9	c	18745	V.L.	f	53	n	n	n
10	c	4674	C.F.	f	66	n	n	n
11	c	2803	W.M.	m	63	y	n	y
12	c	7221	M.K.	f	68	n	n	y
13	c	21817	M.P.	f	32	n	n	n
14	c	7062	S.G.	f	42	y	y	y
15	c	13624	J.M.	f	24	n	n	y
16	c	8217	M.G.	f	84	n	n	n
17	c	22767	J.D.	f	22	n	n	n
18	c	11234	B.Z.	f	67	y	n	y
19	c	8556	I.B.	f	37	n	n	n
20	c	12003	I.L.	f	59	n	n	y
21	c	16227	J.F.	f	64	n	n	n
22	c	17166	A.S.	f	52	n	n	y

c = completed as intended according to study protocol (PP)

Appendix D

Table: D1	Day 4, 15 min	Study-No.: 13.0330-02
Parameter: Visual Score		Parameter-ID: 43854

Pan. # \ Prod.	A	B	C	D	E
1	0	0.5	0	0	0
2	0	0.5	0	0	0
3	0	0	0	0	0
4	0	0	0	0	0
5	0	1	0	0	0
6	0	1	0	0	0
7	0	0	0	0	0
8	0	1	0	0	0
9	0	0.5	0	0	0
10	0	1	0	0	0
11	0	2	0	0	0
12	0	0	0	0	0
13	0	0	0	0	0
14	0	1	0	0	0
15	0	0.5	0	0	0
16	0	1	0	0	0
17	0	0.5	0	0	0
18	0	0	0	0	0
19	0	0.5	0	0	0
20	0	0.5	0	0	0
21	0	0	0	0	0
22	0	0.5	0	0	0
Mean	**0.0**	**0.5**	**0.0**	**0.0**	**0.0**
SD	0.0	0.5	0.0	0.0	0.0
n	22	22	22	22	22

Table: D2	Day 5	Study-No.: 13.0330-02
Parameter: Visual Score		Parameter-ID: 43853

Pan. # \ Prod.	A	B	C	D	E
1	0	0.5	0	0	0
2	0	1	0	0	0
3	0	0.5	0	0	0
4	0	0	0	0	0
5	0	1	0	0	0
6	0	0.5	0	0	0
7	0	0	0	0	0
8	0	0.5	0	0	0
9	0	0.5	0	0	0
10	0	0.5	0	0	0
11	0	2	0	0	0
12	0	0	0	0	0
13	0	0	0	0	0
14	0	0	0	0	0
15	0	0	0	0	0
16	0	0.5	0	0	0
17	0	0.5	0	0	0
18	0	0	0	0	0
19	0	0.5	0	0	0
20	0	0.5	0	0	0
21	0	0	0	0	0
22	0	0.5	0	0	0
Mean	**0.0**	**0.4**	**0.0**	**0.0**	**0.0**
SD	0.0	0.5	0.0	0.0	0.0
n	22	22	22	22	22

Table: D3		**Day 6**			**Study-No.: 13.0330-02**
Parameter: Visual Score					**Parameter-ID: 43852**
Pan. # \ Prod.	A	B	C	D	E
1	0	0.5	0	0	0
2	0	0.5	0	0	0
3	0	0	0	0	0
4	0	0	0	0	0
5	0	0.5	0	0	0
6	0	0.5	0	0	0
7	0	0	0	0	0
8	0	0	0	0	0
9	0	0	0	0	0
10	0	0.5	0	0	0
11	0	1	0	0	0
12	0	0	0	0	0
13	0	0	0	0	0
14	0	0	0	0	0
15	0	0	0	0	0
16	0	0	0	0	0
17	0	0.5	0	0	0
18	0	0	0	0	0
19	0	0.5	0	0	0
20	0	0	0	0	0
21	0	0	0	0	0
22	0	0.5	0	0	0
Mean	**0.0**	**0.2**	**0.0**	**0.0**	**0.0**
SD	0.0	0.3	0.0	0.0	0.0
n	22	22	22	22	22

Appendix E

Table: E1	**Mean Score / all evaluation time points**				**Study-No.: 13.0330-02**
Parameter: Visual Score: Mean Score					**Formula-ID: 5/14345**
Pan. \ Prod.	A	B	C	D	E
1	0	0.5	0	0	0
2	0	0.7	0	0	0
3	0	0.2	0	0	0
4	0	0	0	0	0
5	0	0.8	0	0	0
6	0	0.7	0	0	0
7	0	0	0	0	0
8	0	0.5	0	0	0
9	0	0.3	0	0	0
10	0	0.7	0	0	0
11	0	1.7	0	0	0
12	0	0	0	0	0
13	0	0	0	0	0
14	0	0.3	0	0	0
15	0	0.2	0	0	0
16	0	0.5	0	0	0
17	0	0.5	0	0	0
18	0	0	0	0	0
19	0	0.5	0	0	0
20	0	0.3	0	0	0
21	0	0	0	0	0
22	0	0.5	0	0	0
Mean	**0.00**	**0.40**	**0.00**	**0.00**	**0.00**
SD	0.00	0.39	0.00	0.00	0.00
n	22	22	22	22	22

Appendix F

STUDY PROTOCOL

3 x 24 h Patch Test (02-3x24h-PT) according to Standard Protocol-V03

Further details of the test procedure not described in this Study Protocol are explained in the Standard Protocol-V03

Sponsor SpaBalancer GmbH, Halstenbek

Sponsor Contact Tim Dörries

Sponsor Study-No. -

Study Site proDERM Institut für Angewandte Dermatologische Forschung GmbH, Schenefeld/Hamburg

Medical Director Prof. Dr. med. Klaus-Peter Wilhelm, Dermatologist

Director Research Dipl. Bio-Ing. Stephan Bielfeldt

Project Manager/ Investigator Dipl.-Biol. Christiane Röck

proDERM Study-No. 13.0330-02

Test Dates November 04 to November 09, 2013

Final Report Approximately 3 weeks after completion of the study.

Test Materials

Code/ proDERM	Product/Code/Sponsor	Concentration	Dilution to be done by: (Please tick)	
			pro-DERM	Spon-sor
A	Aqua demin. (Negative control)	as is	-	-
B	Sodium Dodecyl Sulfate (SDS) (Positive control)	0.3 % (w/w)	X	-
C	SpaBalancer	40 ml / 1000 l	-	X
D	SpaBalancer Ultrashock	40 ml / 1000 l	-	X
E	Mixture of SpaBalancer and Ultrashock	1 part C : 1 part D	X	-

Application Volume 25 µl

Patch Test System Haye's Test Chamber®, HAL (occlusive)

Subjects A minimum of 22 subjects will be recruited for this study so that at least 20 subjects are expected to finish this study.

Quality Assurance The study will be conducted, the analysis performed and the report prepared approximating the main principles of Good Clinical Practice (GCP), and in accordance with relevant national regulations, and approved protocol(s). The principle requirements of the Declaration of Helsinki will be taken into account to protect the rights, safety and well-being of subjects participating in the study.

An independent quality assurance unit will be engaged to audit clinical research studies to identify, evaluate and communicate the state of

compliance with applicable protocol(s), and the quality system of proDERM. The audit schedule approved by management will ensure that study specific and system audits will be performed at regular intervals. Objective evidence pertaining to the correct conduct of studies, the performance of quality control measures for completeness and accuracy of clinical research data, data analysis, and reporting of results will be given and reported to management and to the investigator, as appropriate.

Sponsor Inspections/ Audits

The Sponsor may, upon appointment, visit the Study Center at any time during and after the study.

Amendments/ Deviations

None

Protocol approved:

Date:

Date: October 14, 2013

Tim Dörries
SpaBalancer GmbH

C Röcke

Dipl.-Biol. Christiane Röck
- Project Manager/Investigator -
proDERM

Innocuousness Certification for Test Materials

(Not applicable, if an appropriate document will be sent to proDERM)

We herewith confirm that all test materials including references and control materials conform to European Cosmetic Regulation (in the case of cosmetics), or contain only food products in legally accepted quantities (in the case of dietary supplements).

We further confirm that we have sufficient evidence for the innocuousness of the test materials, of the dietary security (for food supplements) and that the test materials present no foreseeable health risks for the panelists taking part in the study under the conditions as defined in the study protocol and its amendments.

Date:

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Tim Dörries
SpaBalancer GmbH

Sachbearbeite

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Position