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REPORT: COMPATIBILITY STUDY

SINGLE PATCH TEST

CLINICAL STUDY FOR THE VERIFICATION OF THE GOOD CUTANEOUS COMPATIBILITY OF A COSMETIC INVESTIGATIONAL PRODUCT AFTER A SINGLE APPLICATION TO THE SKIN OF THE BACK AND UNDER OCCLUSIVE PATCH FOR 48 HOURS, IN THE ADULT SUBJECT

INVESTIGATIONAL PRODUCT
BL138 BİOBELLİNDA 30SPF BODY LOTION (fla n° 02 - batch n° 02)

I.E.C. CODE PRODUCT NUMBER	B160472 01118 164
STUDY PROTOCOL	N° PTS01P1PE - Version 1, of 9 January 2013
SPONSOR	**PIM EGITIM DANISMANLIK**
MANUFACTURER	**BİOBELLİNDA KOZMETİK VE TEMİZLİK ÜRÜNLERİ PAZARLAMA A.Ş**
REPORT	B160472RD1 - Version 1, of 8 April 2016
BEGINNING OF OBSERVATIONS	21 March 2016
END OF OBSERVATIONS	23 March 2016

STUDY MONITOR	DEPUTY TECHNICAL AND SCIENTIFIC MANAGER	DERMATOLOGIST INVESTIGATOR
Mrs S. KAPAR **PIM EGITIM DANISMANLIK** Gokturk Caddesi Suvenue Sitesi No. 2 B Blok K. 3 D. 7 Gokturk ISTANBUL - TURKEY	Mrs E. ATANASSOVA Engineer in Biotechnology, Master in Biotechnology **IEC Bulgarie** Lozenetz - 8/10, Kichinev street 1407 SOFIA - BULGARIA	E. LICHEVA, M.D. **Address of Investigations:** **IEC Bulgarie** Lozenetz – 9/11, Kichinev street 1407 SOFIA - BULGARIA

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AUTHENTICATION

The study subject of the present report was conducted under my responsibility, in compliance with the study protocol, and in accordance with I.E.C. Standard Operating Procedures and in the spirit of the general principles of the Good Clinical Practices.

I have read this report and I agree with its content.

Elenka LICHEVA, M.D.
Dermatologist Investigator

All observations and numerical data obtained during this study are reported in the present document. I have read this report, I certify that these data are an accurate reflection of the results obtained and I agree with its content.

Elitsa ATANASSOVA
Deputy Technical and Scientific Manager

P R O T O C O L	
STUDY TYPE	Compatibility ("single patch test"), under Dermatological Control.
STUDY OBJECTIVE	To verify the good cutaneous compatibility of a cosmetic investigational product after a single application, to the skin of the back and under occlusive patch for 48 hours, in the adult subject.
STUDY RELEVANCE	Cutaneous irritation can be defined as an attack to skin integrity, with lesions to the epidermis and coming from an inflammatory reaction of the dermis, expressed by macroscopically visible phenomena, mainly redness (erythema), up to edema. In Man, the study called "Single Patch Test" (occlusive application of a product to the skin, for 48 hours), allows to check, in 10 to 20 subjects, the good cutaneous compatibility (absence of any primary cutaneous irritation) after a single application followed by a macroscopic examination performed according to a given numerical scale.
INCLUSION CRITERIA *(in addition to the standard criteria defined in the I.E.C. procedures)*	. Number of subjects: 10 . Sex: male or female . Age: 18 to 70 years old . Origin: Caucasian . Healthy subjects with history of atopy: 25%* maximum ** proportion commonly admitted for this population*
METHODOLOGY	**- Application modalities of the investigational product:** . area: back, between the hips and the shoulders . quantity: 0.02 ml over a surface of 50 mm² (occlusive patch "Small Finn Chambers on Scanpor"). . application conditions: investigational product as supplied, under occlusive patch (Patch "AK-8" of Small Finn Chambers on Scanpor type). . frequency and duration: single application, for about 48 hours **- Evaluation modalities:** . clinical observations, about 30 minutes after removal of the patches: readings done compared to those obtained with the "negative" control (patch alone). . cutaneous irritation quantification, according to a given numerical scale (erythema, edema, papulae / vesicles / bullae / pustules, dryness / desquamation, detergent effect, reflectivity), by the method of the differences (product - control).
DATA ANALYSIS	- Determination of the index of Primary Cutaneous Irritation (P.C.I.); mean of the weighted sum of scoring obtained on the whole panel (erythema: factor 1; edema, papulae: factor 2; dryness, detergent effect, reflectivity: factor 0.5). - Interpretation of the results obtained, under the experimental conditions employed, based on : . the P.C.I. obtained . the type of investigational product . the statistics of I.E.C. based on about 10.125 tested products from 1997 to 2007 (safety positioning compared to the products of the same type)

RESULTS AND CONCLUSION

STUDIED POPULATION

Number of subjects recruited	11
Number of subjects who came to I.E.C.	11
Number of subjects included by the Dermatologist Investigator	11
Number of subjects discontinued from the study	0
Number of subjects for the analysis of the results	11

TABLE I
SUBJECTS' CHARACTERISTICS

SUB. N°	CODE	AGE (years)	SEX*	PHOTOTYPE
01	HRINA06	48	F	III
02	TODRO02	52	F	III
03	ACHPA	49	F	III
04	OSTBO	53	F	III
05	TODTA	44	F	III
06	DIMST03	34	F	III
07	PEEHR	22	M	III
08	DIMDI21	27	F	III
09	STOEL04	64	F	III
10	BABZH	60	F	III
11	KASZL	50	F	II

* M = male
F = female

TABLE II
RESULTS OF OBSERVATIONS AND CLINICAL EXAMINATIONS

SUB. N°	ERYTHEMA	EDEMA	PAPULAE/ VESICLES/ BULLAE/ PUSTULES	DRYNESS/ DESQUAMA-TION	DETERGENT EFFECT	REFLECTIVITY
01	0	0	0	0	0	0
02	0	0	0	0	0	0
03	0	0	0	0	0	0
04	0	0	0	0	0	0
05	0	0	0	0	0	0
06	0	0	0	0	0	0
07	0	0	0	0	0	0
08	0	0	0	0	0	0
09	1	0	0	0	0	0
10	0	0	0	0	0	0
11	0	0	0	0	0	0
Weighting	*1*	*2*	*2*	*0,5*	*0,5*	*0,5*

WEIGHTED TOTAL	1

PRIMARY CUTANEOUS IRRITATION INDEX (P.C.I. #)	**0.1**

 # = weighted total / number of subjects

Other observation:
Nothing to report.

CONCLUSION

From the results obtained under the experimental conditions adopted (single application to the skin of the back and under occlusive patch for 48 hours), the CUTANEOUS COMPATIBILITY of the investigational product designated as "BL138 BİOBELLİNDA 30SPF BODY LOTION (fla n° 02 - batch n° 02)", in the adult subject, may be judged, GOOD.

Sofia,
8 April 2016

E. LICHEVA, M.D.
Dermatologist Investigator

E. ATANASSOVA
Deputy Technical and Scientific Manager

This study was conducted by INSTITUT D'EXPERTISE CLINIQUE - BULGARIE,
registered by the Bulgarian Health Authorities
Professor Rumyana YANKOVA, MD., Ph. D., Head of the Dermatology
and Allergology Department of Plovdiv Medical University

QUALITY COMPLIANCE

This study was performed in conformity with the Standard Operating Procedures of the Institut d'Expertise Clinique, the protocol signed with the sponsor and "in the spirit" of the general principles of the Good Clinical Practices published by I.C.H. (Topic E6 : CPMP/ICH/135/95).

Audits of clinical studies are conducted every 6 months on each type of study. They are intended to verify the correct respect of the procedures during the study. The results of these audits are subject to reporting to the Investigator(s) and the Head of Laboratories.

I.E.C. Bulgarie Quality Unit confirms the compliance of this report with the data generated during the study.

Sofia,
8 April 2016

Elena GANCHEVA
Quality Auditor

PROTOCOL COMPLIANCE

No incident which could have affected the quality or the interpretation of the results obtained was observed.

STORAGE OF THE INVESTIGATIONAL PRODUCT

The investigational product was kept under lock and key, from heat (between + 5°C and + 25°C) and from light.

A sample of the investigational product will be kept in our facilities for 4 months as of the date of dispatch of the final report. From this date on, and with no contrary advice of the Sponsor, the investigational product will be destroyed.

DATA RECORDING AND ARCHIVING

Raw data are defined as original records and certified copies of original records of clinical/instrumental findings and observations (hand-written data, printing tickets, pictures, digital recordings, samples…) directly input in the case report form (constituted, paginated and stapled before the start of the study) or in another specific software/folder/file. Raw data are then synthetized in compilation documents, which are mainly informatics files and enable either direct analysis of the data, or transferred to more specific software (video/image analysis, statistical analysis…). If corrections of the raw data or of the compilation are required, the person in charge of the correction shall state the reason, date and sign, according to our procedure (the original entry must remain legible).

All raw data as well as the original documents of the compilation, of the final protocol (amendments if any), of the final report (all different versions and/or amendments if any) and of the statistical analysis if any, will be kept in the archives of I.E.C. for 10 years, at the following addresses:

”Reisswolf - Bulgaria” S.A. - Logistics Park Bozhurishte, 10 Evropa Blvd.
2227 Bozhurishte – Bulgaria.

The traceability of the documents will be the responsibility of I.E.C., who will keep updated records of their archiving address. Once this period is over, the Manufacturer will be contacted regarding its archives. No archive destruction will be done without the written and signed agreement from the Manufacturer.

APPENDIX

EVALUATION SCALE OF CUTANEOUS IRRITATION

EVALUATION SCALE OF CUTANEOUS IRRITATION

ERYTHEMA	
No erythema	0
Very slight erythema (hardly visible) on at least ¾ of the application area, or well visible on a smaller area	1
Clearly visible erythema uniformly allocated on at least ¾ of the application area	2
Severa erythema (dark red)	3
Purpuric erythema	4
EDEMA	
No edema	0
Very slight edema and palpable on at least ¾ of the application area, or slight edema on a smaller surface	1
Slight edema (edges well defined) on at least ¾ of the application area	2
Severe edema (1 mm tick at least) on a surface greater than the application area	3
PAPULAE/VESICLES/BULLAE/PUSTULES	
No papulae, vesicles, bullae, pustules	0
Papulae or small vesicles (less than about 1 mm in diameter)	1
Vesicles 1 to 2 mm in diameter	2
Pustules	3
Bullae with clear liquid	4
DRYNESS/DESQUAMATION	
No dryness or desquamation	0
Slight dryness = mat, unpolished aspect, on at least ¾ of the application area, or pulverulent (whitish) aspect on a surface smaller than ¾ of the application area	1
Clear dryness = pulverulent aspect on at least ¾ of the application area, or desquamatory aspect on a surface smaller than ¾ of the application area	2
Moderate desquamation = desquamatory aspect on at least ¾ of the application area, or presence of thick squamae on a surface smaller than ¾ of the application area	3
Severe desquamation = presence of thick squamae or at least ¾ of the application area, with possibility or tegument fissuration	4
DETERGENT EFFECT	
No rugosity	0
Slight rugosity = slightly worn aspect on at least ¾ of the application area, or clearly worn aspect on a surface smaller than ¾ of the application area	1
Clear rugosity = clearly worn aspect on at least ¾ of the application area, or very worn aspect (presence of wrinkles with well pronounced crests) on a surface smaller than ¾ of the application area	2
Moderate rugosity = very worn aspect on at least ¾ of the application area or presence of deep wrinkles on a surface smaller than ¾ of the application area	3
Severe rugosity = presence of deep wrinkles on at least ¾ of the application area	4
REFLECTIVITY	
No reflectivity	0
Slight reflectivity = slight shiny aspect on at least ¾ of the application area, or clearly shiny aspect on a surface smaller than ¾ of the application area	1
Clear reflectivity = shiny aspect on at least ¾ of the application area, or varnished aspect on a surface smaller than ¾ of the application area	2
Moderate reflectivity = glossy aspect on at least ¾ of the application area or glazed aspect on a surface smaller than ¾ of the application area	3
Severe reflectivity = glazed aspect, deeply shimmering, on at least ¾ of the application area	4

N.B.: Any other abnormality (epidermal erosion, subjective sensations: pruritus, pricking, burning sensation…) was also noted.