EL-170717398CF102-02

Clinical Trial Summary

A Clinical Study for Determining the Sun Protection Factor of ‘more and more mineral sun cream’

(According to Cosmetics Europe (ISO 24444))

September 29, 2017

Ellead Co., Ltd.

Ellead
Skin & Bio Research

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Summary of Clinical Study

Study title	A Clinical Study for Determining the Sun Protection Factor of 'more and more mineral sun cream'	
Study number	EL-170717398CF102-02	
Requestor	Korea Kolmar Co., Ltd.	
Research organization	Ellead Co., Ltd. 7&8 fl., 325, Hwangsaeul-ro, Bundang-gu, Seongnam-si, Gyeonggi-do, Korea	
Duration of study	August 24, 2017 - September 29, 2017	
Name of test product	more and more mineral sun cream	
Formulation	Cream	
Test method	Cosmetics Europe (ISO 24444) and Ellead SOP (EL-P-7400)	
	Test volunteers	Ten (10) generally healthy male and female volunteers aged 18 - 60
	Source of UV radiation	Multi-port Solar Simulator 601-300W with xenon arc lamp
	Reference sunscreen	P2
	Amount & Area of applying	2 ㎎/㎠ & 35 ㎠
	Drying time	15 to 30 minutes
	Time of assessment	20 ± 4 hours
	Calculation of SPF value	Arithmetical mean of all valid individual SPF value
	Verification of reliability	Comparison between 95% confidence interval and ± 17% of mean SPF value
Date of report completion	September 29, 2017	
Result	SPF 70.5 ± 12.4	
President	Kyung Soo Byun (Sign)	
Research director	Nam Soo Kim, M.D., Ph.D. (Sign)	
QA director	You Sun Kim, Ph.D. (Sign)	
Researcher	Hyun Ji Lee, M.S. / So Hee Sung, M.S. / In Hyung Jung, M.S. / Hye Min Ahn, M.S. / So Eun Yoo, M.S. / Ha Na Na, M.S. / Da Jeong Lee, B.A.	

Study Contents

1. Objective

This study has the intention of evaluating the effectiveness of the test product as a sunscreen product on human skin in compliance with Cosmetics Europe (ISO 24444) and Ellead Standard Operating Procedures (EL-P-7400).

2. Duration of Study

August 24, 2017 - September 29, 2017

(Actual test period: August 30, 2017 - September 27, 2017)

3. Research Organization

Ellead Co., Ltd.
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4. Requestor

Korea Kolmar Co., Ltd.

Homepage: www.kolmar.co.kr

5. Information of Test Product

1) Name of test product: more and more mineral sun cream

2) Test product code: M-170717398CF102-02

3) Requestor: Korea Kolmar Co., Ltd.

4) Formulation: Cream

5) Color: Ivory

6) Active ingredient

Active ingredient name	Content (%)
Titanium Dioxide(35%)* C12-15 Alkyl Benzoate*Aluminum Stearate* Polyhydroxystearic Acid*Alumina (as Titanium Dioxide)	20.00 (7.00)
Titanium Dioxide(49.5%)* Caprylic/Capric Triglyceride*Polyhydroxystearic Acid* Alumina*Stearic Acid (as Titanium Dioxide)	2.00 (0.99)

The above list of active ingredients and contents was provided by the requestor.

7) Management and storage of the test product

Upon arrival at Ellead Co., Ltd., the test products are assigned code numbers. The recipient, date and code number are recorded in test product management card. After completion of the study, the test products are retained for a period of 5 years.

Study Methods

This study was performed in accordance with Cosmetics Europe (ISO 24444) and Ellead SOP (EL-P-7400).

Before test	Volunteer recruitment
Test day 1	Fill out Case Report Form Investigation of skin type 1st UV radiation of non-application
Test day 2	1st evaluation for the MED of non-application ($MEDu_1$) UV radiation of test product application 2nd UV radiation of non-application
Test day 3	2nd evaluation for the MED of non-application and test product ($MEDu_2$, MEDp)
After test	Data analysis Evaluation for sun protection effect Prepare data summary sheet Prepare report

1. Principle of Volunteer Selection

1) Inclusion criteria

We selected healthy volunteers (18 - 60 years old) satisfying the following conditions.

- Volunteers falling under the skin types I, II, and III based on Table 1. Fitzpatrick's Skin Classification
- Volunteers who have read, understood and signed informed consent forms
- Volunteers who are healthy and do not have diseases

Table 1. Fitzpatrick's Skin Classification

Types	Description
I	Always burns easily; never tans
II	Always burns easily; tans minimally
III	Burns moderately; tans gradually
IV	Burns minimally; always tans well
V	Rarely burns; tans profusely
VI	Never burns; deeply pigmented

2) Exclusion criteria

- Individuals who are under a doctor's care
- Individuals taking medication which, in the opinion of the investigator, would mask or interfere with the results
- Individuals with chronic skin allergies
- Individuals with suntan or sunburn
- Individuals with abnormal reaction to the sun
- Pregnant or lactating females

3) Informed consent

A signed informed consent was obtained from each volunteer prior to the initiation of the study. The informed consent form describes the study objective, possible adverse effects, associated risks and potential benefits of treatment and the limits of liability. Each volunteer filled in the informed consent honestly, in confidentiality. The signed consent forms are available for inspection on the premises of Ellead Co., Ltd., only.

4) Data rejection criteria

Volunteers' results were rejected and the volunteer was replaced if:

- The responses on the treated test site were randomly absent or out of sequence.
- A Minimal Erythema Dose (MED) could not be obtained due to elicited response at all exposure sites.
- The exposure series failed to elicit an MED response on either the untreated or the applied skin areas. The test was then considered a technical failure and the volunteer's data was discarded.

2. Determination of Ultraviolet Source

1) UV radiation source

Xenon arc Multi-port Solar Simulator 601-300W (Solar Light, USA)

2) Filter

Dichroic filter: obtain selectively the light of 290-400 ㎚ wavelength

UG11 filter: pass only the wavelength of 290-400 ㎚

WG320 filter: eliminate the wavelength of UVC

3) Radiometer

PMA2100 meter and PMA2108 UVB detector (Solar Light, USA)

3. Application

1) Application areas

35 ㎠ (7 ㎝ × 5 ㎝)

2) Waiting period between the application and the UV exposure

15 to 30 minutes

3) Application dose

2 ㎎/㎠

4) Distance between borders of each exposure sub-site

0.8 ㎝

5) Distance between exposure sub-site and edge of the test site

1 ㎝

6) Modes of application

100 ㎕ of the product was weighed in the balance using a Micro pipette (Gilson, USA) and then the volume of the product equivalent to 70 ㎎ was calculated. The product was tapped and spread over the whole application area using a finger with a finger cot.

4. Radiation of Ultraviolet

1) Test area

The individual test site should be within the region between the scapula line and waist. Skeletal protrusions and extreme areas of curvature should be avoided.

2) Radiation area per port

0.64 ㎠

3) Intensity of UV rays and irradiation fixing

In this study, the intensity of UV rays irradiated from the solar simulator was fixed but the time of irradiation was adjusted to control the dose of UV rays for convenience and to save time. If expected SPF value was less than or equal to 25, port no.1 was fixed at 290 ㎼/㎠ and test product site was exposed with incremental UV doses using a geometric progression of 25%.

If expected SPF value was greater than 25, port no.1 was fixed at 445 ㎼/㎠ and test product site was exposed with incremental UV doses using a geometric progression of 15%. Both before irradiation and afterward, the intensity of UV rays was checked with the radiometer for consistent UV output.

4) Progression of the irradiation doses

(1) Non-application MED (MEDu) measurement

290 ㎼/㎠ was set as the initial value for port no.1 and it was increased by 25% in geometric ratio as the port number was increased. For determining MEDu, 15.0 mJ/㎠ was radiated from port no.1 by controlling irradiation time. On the first day of the test, non-application MED ($MEDu_1$) was measured by the former irradiation doses. On the second day, non-application MED ($MEDu_2$) was measured. In this manner the actual $MEDu_2$ exposed was calculated.

(2) MED measurement of reference sunscreen (P2)

The pre-calculated value of $MEDu_1$ was set to locate on port no.4. The expected SPF index value of the reference sunscreen was hypothesized to be 16. Then, the quantity of light calculated using the value of expected SPF index value at port no.4 was divided by the intensity of UV ray (566 ㎼/㎠).

(3) MED (MEDp) measurement of test product

The same procedures as the reference sunscreen were taken.

5. Determination of SPF value

1) Evaluation of responses

The MED was assessed by visual comparison by two researchers 16 to 24 hours after exposure using the following scoring system.

O = Negative, no visible erythema reaction

± = Undefined erythema reaction

+ = Defined erythema reaction

++ = Moderate clearly defined erythema reaction

+++ = Marked erythema reaction

2) Calculation of SPF value

The SPF values for the reference sunscreen and test product were calculated as follows:

$$\text{SPF value} = \frac{\text{MED in protected skin (MEDp)}}{\text{MED in unprotected skin (MEDu}_2\text{)}}$$

3) Reliability

The 95% confidence interval of SPF value was calculated using the following equation, and the experiment was considered valid when the confidence interval fell within ± 17% of the mean SPF value of 10 volunteers. If the 95% confidence interval did not fall within ± 17% of the mean SPF value, the number of volunteers was increased or the experiment conditions were adjusted in principle.

95% confidence interval = (SPF - C) ~ (SPF + C)

$$C = t\ value \times \frac{S}{\sqrt{n}}$$

$t\ value$: $t\ value$ from the 'two-sided' Student t distribution table at a probability level $p=0.05$ and with degrees of freedom $v=(n-1)$

n: total number of volunteers

S: standard deviation

6. Archiving

All original products, raw data, technician's notebooks, correspondence files, copies of final reports and remaining specimens are maintained on the premises of Ellead Co., Ltd.

7. Reference Sunscreen (P2)

The reference sunscreen used in this experiment was made according to the method of manufacturing reference sunscreen of SPF proposed by Cosmetics Europe (ISO 24444) and Ellead SOP (EL-P-7400).

	Ingredients	% (w/w) (% weight of total weight)
Phase 1	lanolin	4.5
	theobroma cacao (cocoa) seed butter	2.0
	glyceryl monostearate	3.0
	stearic acid	2.0
	ethylhexyldimethyl PABA (CAS 21245-02-3) (2-ethylhexyl-4-(dimethylamino)-benzoate)	7.0
	benzophenone-3 (CAS 131-57-7)	3.0
Phase 2	water	71.6
	sorbitol (liquid 70%)	5.0
	triethanolamine	1.0
	methylparaben	0.3
	propylparaben	0.1
Phase 3	benzyl alcohol	0.5

The SPF value of the reference sunscreen is 16.1 ± 2.4.

Results

1. Results of Pre-test

Ellead Co., Ltd. conducted the pre-test for determining the SPF value of test product with expected SPF value 50.

Volunteer number	Age	Sex	Skin type†	MEDu2 (mJ/㎠)	Reference sunscreen SPF value	Test product SPF value
S17-651	39	F	III	36.8	16.0	57.5
S17-653	23	F	III	29.4	16.0	57.4
S17-654	21	F	III	23.8	15.9	65.5
Mean				**30.0**	**16.0**	**60.2**

† The skin type of a volunteer is determined based on the survey and the results of MED without the application of a sunscreen agent.

The pre-test SPF value of the test product was determined to be 60.2. Accordingly, we conducted the study with expected SPF value adjusted to 60.

2. Results of Test

Volunteer number	Age	Sex	Skin type	$MEDu_2$† (mJ/㎠)	Reference sunscreen SPF value	Test product SPF value
S17-708	21	F	II	18.7	16.2	69.7
S17-709	53	M	III	18.7	16.2	69.7
S17-710	25	M	III	23.4	12.9	55.7
S17-711	50	M	III	23.4	16.2	64.1
S17-712	56	F	III	23.8	15.9	78.7
S17-713	55	F	III	23.6	15.9	74.8
S17-714	24	M	III	23.4	16.2	64.1
S17-715	26	M	III	19.0	15.9	64.9
S17-716	57	F	II	14.9	16.2	100.6
S17-717	43	F	III	36.8	12.8	63.4
Total	Mean	**F 5**	**Type I 0**	Mean	Mean	Mean
			Type II 2			
10	**41.0**	**M 5**	**Type III 8**	**22.6**	**15.4**	**70.5**
				Std.	Std.	Std.
				5.9	**1.4**	**12.4**

† These values are only for determining MED using the light source and radiometer limited to this study. Thus they are not compatible with those from other studies using different light sources and radiometers.

	Mean	Standard deviation	Volunteer number (n)	*t value*	17% interval of mean	95% confidence interval	Validity of test
Reference sunscreen	**15.4**	**1.4**	**10**	**2.262**	**2.6**	**1.0**	**Valid**
Test product	**70.5**	**12.4**	**10**	**2.262**	**12.0**	**8.8**	**Valid**