STUDY PROTOCOL

Skin Enhancement & Skin Repair Efficacy Clinical Study

Research Center	**Shanghai China-Norm Quality Technical Service Co., Ltd.**
Study-No.:	**C210579 (CRO)** **CN-CLI-21-14049-46 (Sponsor)**
Investigational Product:	**Facial Serum [Formula# 899467 14]**
Sponsor:	**L'Oréal R&I CHINA**
Date of Protocol:	**November 16th, 2021, Version 4.0-final**
Study Duration	**December 8th, 2021 ~ 28th January, 2022**

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1. Responsibilities

The management system of CRO is certified for the scope "Cosmetic Testing". Study performance, data analysis and study report are based on the Quality Management System ISO 9001:2015.

The study report represents a correct description of measured values and recorded results during the study. To the best of its knowledge, CRO ensures the absence of significant deviations from the study protocol affecting the quality/integrity of this study.

Study performance, data analysis, and study report are realized approximating the main principles of GCP.

Principle requirements of the Declaration of Helsinki are taken into consideration.

Shanghai China-Norm Quality Technical Service Co., Ltd

L'Oréal R&I CHINA

Xingzuo LAI

2. General Information

Title:	Skin Enhancement & Skin Repair Efficacy Clinical Study
Study Number:	C210579 (CRO) CN-CLI-21-14049-46 (Sponsor)
Test Product:	Facial Serum [Formula# 899467 14]
Principal Investigator:	Dr. Ma Title: Dermatologist Tel: +86 021 55971185 Fax: +86 021 55971185
Test Site:	China-Norm U@Test laboratory Address: 310, Building #13, No.697, Lingshi Road, Health Work, Jing' an District, Shanghai, China
Study Objective:	To evaluate the effect of a facial essence on skin barrier and skin condition after 2-week of use; And study on the repair efficacy of skin barrier and condition after receiving Fractional Ultrapulse CO_2-laser. The whole study will be divided into two dimensions to evaluate the product: the comparison of the effect before and after and the comparison with the control group.
Experimental Design:	Mono-centric, single-blind, parallel random and home use design.
Test Areas:	Whole face
Subjects:	70 female adult subjects will be enrolled and divided into 2 groups in the study, recruited according to inclusion and non-inclusion criteria listed below, and at least 60 subjects should complete the whole study (at least 30 subjects per group). - Group 1: Facial Serum Group - Group 2: Non-treatment Group
Age:	20-50 years old
Measurements:	***Clinical Assessment(N=60):*** Skin qualities of skin dryness, erythema, papules, desquamation, chromatosis, edema, escharosis, elasticity, evenness, brightness, radiance, smoothness, pores on cheek, crow's feet wrinkle, epithelial confluence and overall healthy appearance will be evaluated by dermatologist at T0 (baseline), T14d (after pre-treatment), T15d (Timm post-procedure), T16d (1-day after self-recovery), T18d (3-day after self-recovery), T22d (7-day after self-recovery), T25d (10-day after self-recovery and product treatment start), T32d (7-day after product treatment), T39d (14-day after product treatment) for all groups. ***Lactic Acid Stinging Test (N=60)*** Sensitive level by Lactic acid test at T0 (baseline), T14d (after pre-treatment), T25d (10-day after self-recovery and product treatment start), T39d (14-day after product treatment) for all groups. ***Instrument Assessment(N=60):*** - **Corneometer:** skin hydration on both cheeks will be measured at T0 (baseline), T14d (after pre-treatment), T15d (Timm post-procedure), T16d (1-

day after self-recovery), T18d (3-day after self-recovery), T22d (7-day after self-recovery), T25d (10-day after self-recovery and product treatment start), T32d (7-day after product treatment), T39d (14-day after product treatment) for all groups.

- **Vapometer:** transepidermal water loss (TEWL) on both cheeks will be measured at T0 (baseline), T14d (after pre-treatment), T15d (Timm post-procedure), T16d (1-day after self-recovery), T18d (3-day after self-recovery), T22d (7-day after self-recovery), T25d (10-day after self-recovery and product treatment start), T32d (7-day after product treatment), T39d (14-day after product treatment) for all groups.

- **Cutometer:** skin elasticity (R2, R5, R7) on both cheeks will be measured at T0 (baseline), T14d (after pre-treatment), T15d (Timm post-procedure), T16d (1-day after self-recovery), T18d (3-day after self-recovery), T22d (7-day after self-recovery), T25d (10-day after self-recovery and product treatment start), T32d (7-day after product treatment), T39d (14-day after product treatment) for all groups.

- **pH-meter:** skin pH value on both cheeks will be measured at T0 (baseline), T14d (after pre-treatment), T15d (Timm post-procedure), T16d (1-day after self-recovery), T18d (3-day after self-recovery), T22d (7-day after self-recovery), T25d (10-day after self-recovery and product treatment start), T32d (7-day after product treatment), T39d (14-day after product treatment) for all groups.

Photo Capture and Imaging Analysis(N=60):

- **VISIA 7:** standard facial photos shooting will be done at T0 (baseline), T14d (after pre-treatment), T15d (Timm post-procedure), T16d (1-day after self-recovery), T18d (3-day after self-recovery), T22d (7-day after self-recovery), T25d (10-day after self-recovery and product treatment start), T32d (7-day after product treatment), T39d (14-day after product treatment) for all groups.

- **OCT:** standard facial scan will be done at T0 (baseline), T14d (after pre-treatment), T15d (Timm post-procedure), T16d (1-day after self-recovery), T18d (3-day after self-recovery), T22d (7-day after self-recovery), T25d (10-day after self-recovery and product treatment start), T32d (7-day after product treatment), T39d (14-day after product treatment) for all groups.

Self-Assessment(N=60):

- **Self-Assessment Questionnaire on product efficacy** will be answered by subjects at T14d (after pre-treatment), T25d (10-day after self-recovery), T32d (7-day after product treatment), T39d (14-day after product treatment) for Group 1 (N=30);

- **Self-Assessment Questionnaire on cosmeticity** will be answered by subjects at T14d (after pre-treatment), T39d (after product treatment) for Group 1 (N=30).

- **Self-assessment questionnaire on post-procedure tolerance** will be answered by subjects at T15d (Timm post-procedure), T16d (1-day after self-recovery), T18d (3-day after self-recovery), T22d (7-day after self-recovery), T25d (10-day after self-recovery) for all groups (N=60).

Test Duration: 9-visits in 39-days (7-days for washout, 14-days for pre-treatment, 1-day for Chemical procedure, 1-day self-recovery, 3-day self-recovery, 7-day self-recovery, 10-day skin self-recovery and 14-days post-treatment).

- *Visit 1: T-7d*
- *Visit 2: T0 (baseline)*
- *Visit 3: T14d (14-day after pre-treatment)*
- *Visit 4: T15d (Chemical procedure and Timm post-procedure)*
- *Visit 5: T16d (1-day after self-recovery)*
- *Visit 6: T18d (3-day after self-recovery)*
- *Visit 7: T22d (7-day after self-recovery)*
- *Visit 8: T25d (10-day after self-recovery and product treatment start)*
- *Visit 9: T32d (7-day after product treatment)*
- *Visit 10: T39d (14-day after product treatment)*

3. Selection of Volunteers

According to the declaration of Helsinki[1]the subjects must consent to the study in writing. Before-hand they are informed about the study, its objectives, probable benefits, potential risks, and troublesome aspects, as well as about their rights and responsibilities. Volunteers, who fulfil the following criteria of inclusion and exclusion, take part in the study.

Inclusion Criteria:

Prospective subjects meeting all the criteria below will be eligible for enrolment:

1. Chinese women, 20-50 years old;
2. All skin types (dry, normal, oily and mixed);
3. No high risk of hyperpigmentation skin (adjusted by the Hyperpigmentation skin questionnaire refer to Annex 11.2);
4. Rough ad dull skin by self-declared;
5. Lack of radiance, brightness, smoothness by self-claimed;
6. Presenting with problems of acne mark, acne scar or blemishes on face;
7. Did not participate any clinical test or cosmetic product test on skin within 3 months;
8. Did not participate any chemical procedures for previous 2 months; and willing to not participate any procedures during the whole study;
9. No disagreement of dermatologist because of other reasons that exclude the participation of the volunteer.
10. In general good health at the time of the study;
11. Willing and able to participate as evidenced by signing of informed consent;
12. Willing and able to participate the assigned chemical procedure and apply the assigned products;
13. Must be willing to comply with all study protocol requirements (pay attention to: only use the skin care products provided during the study, not take topical or oral treatment like retinol, hormone, anti-oxidant health-care products which may affect the anti-aging efficacy of test serum).

Exclusion Criteria:

Prospective subjects meeting any of the criteria listed below will be excluded from participation:

1. Pregnant or breast-feeding woman or woman planning pregnancy during the study.
2. Subject deprived of rights by a court or administrative order.
3. Major subject to a guardianship order.
4. Subject residing in a health or social care establishment.
5. Patient in an emergency setting.
6. Subject with a skin disease in the test areas as well as skin allergy (particularly e.g., acne, rosacea, eczema).
7. Volunteer presenting a stable or progressive serious disease (per investigator's assessment).
8. Immuno-compromised subject.
9. Subject has hyperpigmentation skin symptoms.
10. Subject with history of allergy to cosmetic or personal care products or ingredients.
11. Subject presenting excessive exposure to sunlight or UV radiation (investigator's assessment).
12. Subjects regularly practicing aquatic or nautical sports.
13. Subjects regularly attending a sauna.
14. Subject with physical highly sensitive constitution;

[1]Declaration of Helsinki, 64th World Medical Assembly, Fortaleza, Brazil, October 2013

15. Subject with cardiovascular or circulatory history.
16. Subject with a history of skin cancer or malignant melanoma.
17. Subject with history of medical beauty treatment and taking part in anti-aging studies in the last 3 months before study.
18. Intake of antihistamines, antibiotics, corticosteroids, non-steroidal anti-inflammatories or immune-suppressants in the last 6 months before study.

4. Study Design

70 female adult subjects will be enrolled and divided into 2 groups in the study, recruited according to inclusion and non-inclusion criteria listed below, and at least 60 subjects should complete the whole study (at least 30 subjects per group).

- ***Clinical Assessment(N=60):***

Skin qualities of skin dryness, erythema, papules, desquamation, chromatosis, edema, escharosis, elasticity, evenness, brightness, radiance, smoothness, pores on cheek, crow's feet wrinkle, epithelial cell confluence and overall healthy appearance will be evaluated by dermatologist at T0 (baseline), T14d (after pre-treatment), T15d (Timm post-procedure), T16d (1-day after self-recovery), T18d (3-day after self-recovery), T22d(7-day after self-recovery), T25d (10-day after self-recovery and product treatment start), T32d (7-day after product treatment), T39d (14-day after product treatment) for all groups.

- ***Lactic Acid Stinging Test (N=60)***

Sensitive level by Lactic acid test at T0 (baseline), T14d (after pre-treatment), T25d (10-day after self-recovery and product treatment start), T39d (14-day after product treatment) for all groups.

- ***Instrument Assessment(N=60):***

- **Corneometer**: skin hydration on both cheeks will be measured at T0 (baseline), T14d (after pre-treatment), T15d (Timm post-procedure), T16d (1-day after self-recovery), T18d (3-day after self-recovery), T22d (7-day after self-recovery), T25d (10-day after self-recovery and product treatment start), T32d (7-day after product treatment), T39d (14-day after product treatment) for all groups.
- **Vapometer:** transepidermal water loss (TEWL) on both cheeks will be measured at T0 (baseline), T14d (after pre-treatment), T15d (Timm post-procedure), T16d (1-day after self-recovery), T18d (3-day after self-recovery), T22d (7-day after self-recovery), T25d (10-day after self-recovery and product treatment start), T32d (7-day after product treatment), T39d (14-day after product treatment) for all groups.
- **Cutometer:** skin elasticity (R2, R5, R7) on both cheeks will be measured at T0 (baseline), T14d (after pre-treatment), T15d (Timm post-procedure), T16d (1-day after self-recovery), T18d (3-day after self-recovery), T22d (7-day after self-recovery), T25d (10-day after self-recovery and product treatment start), T32d (7-day after product treatment), T39d (14-day after product treatment) for all groups.
- **pH-meter:** skin pH value on both cheeks will be measured at T0 (baseline), T14d (after pre-treatment), T15d (Timm post-procedure), T16d (1-day after self-recovery), T18d (3-day after self-recovery), T22d (7-day after self-recovery), T25d (10-day after self-recovery and product treatment start), T32d (7-day after product treatment), T39d (14-day after product treatment) for all groups.

- ***Photo Capture and Imaging Analysis(N=60):***

- **VISIA 7:** standard facial photos shooting will be done at T0 (baseline), T14d (after pre-treatment), T15d (Timm

post-procedure), T16d (1-day after self-recovery), T18d (3-day after self-recovery), T22d (7-day after self-recovery), T25d (10-day after self-recovery and product treatment start), T32d (7-day after product treatment), T39d (14-day after product treatment) for all groups.

- **OCT:** standard facial scan will be done at T0 (baseline), T14d (after pre-treatment), T15d (Timm post-procedure), T16d (1-day after self-recovery), T18d (3-day after self-recovery), T22d (7-day after self-recovery), T25d (10-day after self-recovery and product treatment start), T32d (7-day after product treatment), T39d (14-day after product treatment) for all groups.

- ***Self-Assessment(N=60):***

- **Self-Assessment Questionnaire on product efficacy** will be answered by subjects at T14d (after pre-treatment), T25d (10-day after self-recovery), T32d (7-day after product treatment), T39d (14-day after product treatment) for Group 1 (N=30);

- **Self-Assessment Questionnaire on cosmeticity** will be answered by subjects at T14d (after pre-treatment), T39d (after product treatment) for Group 1 (N=30).

- **Self-assessment questionnaire on post-procedure tolerance** will be answered by subjects at T15d (Timm post-procedure), T16d (1-day after self-recovery), T18d (3-day after self-recovery), T22d (7-day after self-recovery), T25d (10-day after self-recovery) for all groups (N=60).

1) Study Schedule:

Activities	Wash-out	Pre-treatment		Chemical Procedure		10-day Self-recovery			Post-treatment		
	V1	V2	V3	V4		V5	V6	V7	V8	V9	V10
	T-7d	T0 (baseline)	T14d (after pre-treatment)	T15d	T15d-Timm (post-procedure)	T16d (1-day after self-recovery)	T18d (3-day after self-recovery)	T22d (7-day after self-recovery)	T25d (10-day after self-recovery & post-treatment start)	T32d (7-day after post-treatment)	T39d (7-day after post-treatment)
Written informed consent	X										
Inclusion / non-inclusion Criteria (Primary eligibility)	X										
Medical history	X										
Pregnancy test	X										
Clinical grading by dermatologist	X only screening	X	X		X	X	X	X	X	X	X
CO2 laser				X							
VISIA 7		X	X		X	X	X	X	X	X	X
OCT		X	X		X	X	X	X	X	X	X
Lactic acid Sting Test		X	X						X		X
Corneometer		X	X		X	X	X	X	X	X	X
Vapometer		X	X		X	X	X	X	X	X	X
Cutometer		X	X		X	X	X	X	X	X	X
pH meter		X	X		X	X	X	X	X	X	X
Self-assessment QNs			X		X	X	X	X	X	X	X
*Product Application		←	→						←	—	→
*Tolerance feedback in dairy log		←	→						←	—	→
Distribute(D)/Return(R)/Weight(W) Investigational Product (IP) and Standard Product (STD)	X STD(D/W)	X STD/IP(D/W)	X STD/IP(R/W)						X STD/IP(D/W)	X STD/IP(W)	X STD/IP(R/W)
Compliance Check	X	X	X	X	X	X	X	X	X	X	X
AE/SAE Report	X	X	X	X	X	X	X	X	X	X	X
End of Study											X

All the measurements will be conducted under the conditions with a well-controlled room temperature (21± 1 °C) and humidity (45% ± 5 %).
*Double-arrow means the product continuous application for 2-week pre-treatment period and 2-week post-treatment;

5. Measurement

5.1. Clinical Assessment (N=60)

Skin qualities will be evaluated by validated Dermatologist at T0 (baseline), T14d (after pre-treatment), T15d (Timm post-procedure), T16d (1-day after self-recovery), T18d (3-day after self-recovery), T22d (7-day after self-recovery), T25d (10-day after self-recovery and product treatment start), T32d (7-day after product treatment), T39d (14-day after product treatment). Every effort will be made to have the Dermatologist grade the same subjects throughout the study. The Dermatologist will not be allowed to reference previous scores at post-baseline assessments. The half-point scores (0.5) increment may be used when necessary to describe the skin appearance more accurately in Griffith 10-points scale. The tendentious half-point scores (0.4 or 0.6) may be used in scales from Asian skin aging atlas.

- **Skin symptoms post-procedure** include dryness, erythema, papules, desquamation, chromatosis, edema, escharosis will be evaluated.

- **Skin qualities** include the elasticity, skin evenness, skin brightness, skin smoothness, skin radiance, pores on cheeks and over healthy appearance will be evaluated.

Attributes in 6-points scale (0 to 5 scale):

- Dryness (0 to 5, 0 score means no any symptom, 5 score means very serious)
- Erythema (0 to 5, 0 score means no any symptom, 5 score means very serious)
- Papules (0 to 5, 0 score means no any symptom, 5 score means very serious)
- Desquamation (0 to 5, 0 score means no any symptom, 5 score means very serious)
- Chromatosis (0 to 5, 0 score means no any symptom, 5 score means very serious)
- Edema (0 to 5, 0 score means no any symptom, 5 score means very serious)
- Escharosis (0 to 5, 0 score means no any symptom, 5 score means very serious)
- Epithelial cell confluence (0 to 5 scale)
  0=none
  1=very slight (up to 10%)
  2=slight (11%-30%)
  3=moderate (31%-60%)
  4=extensive (61%-90%)
  5=almost complete or complete (91%-100%)

Attributes in Atlas:

- **Crow's feet wrinkles (0 to 6 scale)**

The parameter will be scored according to the Skin Aging Atlas of 0 to 6 on Page 40 to 41.

Attributes in Griffith 10-points scale (0 to 9 scale):

Parameter	Type of Grading	None (Best possible condition) (=0)	Mild (1-3)	Moderate (4-6)	Severe (Worst possible condition) (7-9)
Skin elasticity	Tactile	Skin feels toned, dense and resilient, skin can be snapped back immediately, there are no pressing traces	Elastic but light flabby	Moderate flabby	Skin feels pliable, thin and no-resilient, visible flabby, there are obvious pressing trace
Skin evenness	Visual	Very even tone: no detractions	Slight uneven skin tone: minor detractions covering less than 15%	Somewhat uneven skin tone: detractions covering less than 50%	Uneven, discolored appearance (brown and/or red colors), detractions covering more than 50%

Parameter	Type of Grading	None (Best possible condition) (=0)	Mild (1-3)	Moderate (4-6)	Severe (Worst possible condition) (7-9)
Skin brightness	Visual	Skin is gloss and brightness, there is no darkness and unevenness	Skin is gloss and brightness, there are a little be darkness and unevenness	Skin is moderate degree and visible darkness and unevenness	Skin is extreme and visible darkness and unevenness, there is no gloss and brightness
Skin smoothness	Visual	Perfect smooth, extremely smooth, even-looking skin texture, no roughness	Adequate to acceptable smooth	Perceivable to slight smooth	Rough looking, heave rough; pronouncedly, extensively visible skin roughness
Skin radiance	Visual	Extremely radiant, luminous or glowing appearance all over the tested area	Adequate to acceptable radiance, most area with visibly radiant and glowing appearance	Perceivable to slight radiance	Very slight radiance or extreme dull looking, skin is heavily dull and matte, no luster on face
Appearance of pores on cheek	Visual	Minimal visible pores, adequately smooth on face. Tiny pores or pores are barely seen.	Mild visible pores, small pores are visible on face, but the surface is acceptably smooth	Moderate visible pores, pores are clearly seen in a certain amount on face.	Heavy/extreme visible pores, noticeable pores, large pores or a certain area of pores are visible on face. Skin is quite rough and similar as bare skin
Overall healthy appearance	Visual	Glowing with healthy appearance, energetic-looking	Adequate to acceptable glowing, looks healthier	Perceivable to slight glowing, looks less heathy	Poor, unhealthy appearance

5.2. Lactic Acid Test (N=60)

The lactic acid test is widely accepted as a marker of skin sensitivity and employed for the selection of subjects experiencing invisible sensory irritation. A self-assessment questionnaire (Annex 11.4) of the intensity of symptoms (stinging, itchiness, burning and other) will be answered by subject at 30 seconds, 2.5 minutes, 5 minutes after lactic application. The variation of score between 10% concentration of lactic and distilled water will be calculated and defined to the sensitive level. This process will be done at T0 (baseline), T14d (after pre-treatment), T25d (10-day after self-recovery and product treatment start), T39d (14-day after product treatment)

- Score 0: Not at all
- Score 1: Slight
- Score 2: Moderate
- Score 3: Severe

5.3. Instrumental Assessment (N=60)

The skin hydration by Corneometer CM825, the transepidermal water loss (TEWL) by Vapometer and skin elasticity by Cutometer MPA580 and skin pH by Skin-pH-Meter PH905 under validated technician operation at T0 (baseline), T14d (after pre-treatment), T15d (Timm post-procedure), T16d (1-day after self-recovery), T18d (3-day after self-recovery), T22d (7-day after self-recovery), T25d (10-day after self-recovery and product treatment start), T32d (7-day after product treatment), T39d (14-day after product treatment).

- ***Corneometer CM825 (Courage & Khazaka, Germany)***

It measures moisture content of the skin via capacitance measurements. The measurable capacitance is proportional to the water content of stratum corneum, given that other physical and physiological variables affecting skin electrical properties are carefully controlled. The tested areas on left and right upper cheeks according to *Diagram 1* and the 3M Transparent template will be used for positioning. Consecutive readings will be collected to make sure the variation tolerance is less than ±7; The average of 3 consecutive valid measurements will be calculated.

- ***Vapometer (Delfin Technologies, Finland)***

It's equipped with a closed cylindrical chamber. When it is in contact with the skin, the relative humidity (RH %) in the chamber increases, based on which transepidermal water loss (TEWL) is calculated. Lower

TEWL means better skin barrier function. Vapometer measurement will be done at the tested areas on face skin according to *Diagram 1* and the 3M Transparent template will be used for positioning. One measurement of each test area will be taken.

- ***Cutometer Dual MPA580 (Courage & Khazaka, Germany)***

The measuring principle of the Cutometer® is based on the suction method, in which negative pressure deforms the skin mechanically. The pressure is created in the device and the skin is drawn into the aperture of the probe and after a defined time released again. Inside the probe, the penetration depth is determined by a non-contact optical measuring system. This optical measuring system consists of a light source and a light receptor, as well as two prisms facing each other, which project the light from transmitter to receptor. The light intensity varies due to the penetration depth of the skin. The resistance of the skin to the negative pressure (firmness) and its ability to return into its original position (elasticity) are displayed as curves (penetration depth in mm/time) in real time during the measurement. From these curves a variety of interesting measurement parameters can be calculated related to elastic and visco-elastic properties of skin surface and skin aging.

Before measurement, subject will be asked to lie down on the beauty bed and ensure her head staying in a relatively fixed position across subjects. The standard set-up will be fixed (10s for on-time, 10s for off-time, only 1 time for measurement). Among the generated parameters, repeats average of R0, R2, R5 and R7 will be taken into statistical analyze and all curves should be preserved. The same measurement site will be select according to *Diagram 1*.

- R2(Ua/Uf), the gross elasticity of the skin, including viscous deformation, and is represented by the ratio of "the ability of re-deformation of skin" to "final distension";
- R5(Ur/Ue), the so-called net elasticity of skin without viscous deformation
- R7(Ur/Uf), the biological elasticity.

- ***Skin-pH-Meter PH905 (Courage & Khazaka, Germany)***

This device is a quick, easy, and economical tool to specifically measure the pH on the skin surface or the scalp. The modern, high-quality electronics of the probe allow a very quick (1s) and reliable measurement avoiding occlusion effects. The probe hed is planar for measuring optimally on the skin surface. pH value on scalp is measured on the shaved area and non-shaved area each for one reading at T0.

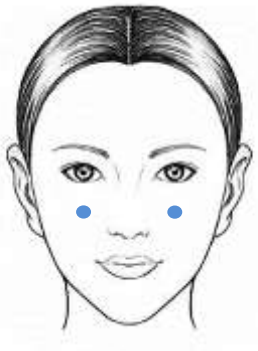

Diagram 1. Test Area for instrumental measurement on both cheeks

5.4. Photo Capture and Imaging Analysis (N=60)

- ***Facial Image Capture by VISIA 7 (Canfield, America)***

Subjects will be asked to wear hair band, close eyes, and coordinate with image-position matching, then take pictures by trained technician. The facial photo is captured by VISIA 7 on front, left and right sides with standard, cross polarized and UV light operated by trained technician at T0 (baseline), T14d (after pre-

treatment), T15d (Timm post-procedure), T16d (1-day after self-recovery), T18d (3-day after self-recovery), T22d (7-day after self-recovery), T25d (10-day after self-recovery and product treatment start), T32d (7-day after product treatment), T39 d (14-day after product treatment).

- ***Optical Coherence Tomography (OCT)（Michelson Diagnostics，England）***

Optical Coherence Tomography (OCT) is a non-invasive imaging technique used to evaluate the retina. The image is acquired using laser light to scan the retina and results in an image that shows the retinal layers in detail. When looking at an OCT scan we see it as if the retina were cut in half and seen from the side. The Optical Coherence Tomography will be operated by trained technician at T0 (baseline), T14d (after pre-treatment), T15d (Timm post-procedure), T16d (1-day after self-recovery), T18d (3-day after self-recovery), T22d (7-day after self-recovery), T25d (10-day after self-recovery and product treatment start), T32d (7-day after product treatment), T39d (14-day after product treatment).

5.5. Fractional Ultrapulse CO_2-laser

The Fractional Ultrapulse CO_2-laser is a gas laser. It generates arrays which act on the dermis and promote the generation of dermal collagen and the rearrangement of collagen fibers. The instrument uses ultrapulse mode and the pulse ejects continuously or repeatedly with a frequency of 1000Hz. The Fractional Ultrapulse CO_2-laser will be operated by medical technologist at T15d (Timm post-procedure).

5.6. Self-assessment Questionnaire (N=60)

- **Self-Assessment Questionnaire on product efficacy** will be answered by subjects at T14d (after pre-treatment), T25d (10-day after self-recovery), T32d (7-day after product treatment), T39d (14-day after product treatment) for Group 1 (N=30);

- **Self-Assessment Questionnaire on cosmeticity** will be answered by subjects at T14d (after pre-treatment), T39d (after product treatment) for Group 1 (N=30).

- **Self-assessment questionnaire on post-procedure tolerance** will be answered by subjects at T15d (Timm post-procedure), T16d (1-day after self-recovery), T18d (3-day after self-recovery), T22d (7-day after self-recovery), T25d (10-day after self-recovery) for all groups (N=60).

6. Product

6.1. Test Products

Product No.	Formula#	Product Name	Label As
Investigational Products			
1	899467 14	Facial serum	上海复硕正态– 电话:+8613641985086 测试编号 C210579 测试精华 配方号：899467 14 用于全脸 50ml/瓶 批号: 生产日期: 室温保存 20-25°C 禁止入口入眼，如不慎入眼，请立即用大量清水冲洗。仅供本测试使用，禁止销售，防止儿童接触。 受试者编号: 产品瓶号:
Support Products			
2	730457 36	Standard cleanser	上海复硕正态– 电话:+8613641985086 测试编号 C210579 标准洁面 配方号：730457 36 用于全脸 其他请看使用说明 125ml/瓶 批号: 生产日期: 室温保存 20-25°C 禁止入口入眼，如不慎入眼，请立即用大量清水冲洗。仅供本测试使用，禁止销售，防止儿童接触。 受试者编号: 产品瓶号:
3	609801 04	Standard moisturization	上海复硕正态– 电话:+8613641985086 测试编号 C210579 标准面霜 配方号：609801 04 用于全脸 其他请看使用说明 40ml/瓶 批号: 生产日期: 室温保存 20-25°C 禁止入口入眼，如不慎入眼，请立即用大量清水冲洗。仅供本测试使用，禁止销售，防止儿童接触。 受试者编号: 产品瓶号:

Product No.	Formula#	Product Name	Label As
4	885218 3	Standard sunscreen	上海复硕正态– 电话:+8613641985086 测试编号 C210579 标准防晒霜 配方号：885218 3 用于全脸 其他请看使用说明 40ml/瓶 批号: 生产日期: 室温保存 20-25°C 禁止入口入眼，如不慎入眼，请立即用大量清水冲洗。仅供本测试使用，禁止销售，防止儿童接触。 受试者编号: 产品瓶号:
5	N/A	Complementary medicines EGF 重组皮肤生长因子	On marketed

6.2. Products Application and Usage Instruction

Mode of application

a. 1-week wash-out stage: T-7d ~ T0 for all groups

A.M.: Standard cleanser + Standard moisturizer + Standard SPF

P.M.: Standard cleanser + Standard moisturizer

b. 2-week pre-treatment stage: T0 ~ T14d

【Group 1-Facial Serum group】

A.M.: Standard cleanser + Test serum + Standard moisturizer + Standard Sunscreen

P.M.: Standard cleanser + Test serum + Standard moisturizer

【Group 2-Non-treatment group】

A.M.: Standard cleanser + Standard moisturizer + Standard Sunscreen

P.M.: Standard cleanser + Standard moisturizer

The standard sunscreen needs to apply to face every morning 15 minutes before sun exposure and re-apply if necessary. Keep out of eyes. No any other skin care or facial make up products are used.

c. 10 days recovery stage: T15d ~ T24d for all groups

A.M.: Sterile saline solution + EGF

P.M.: Sterile saline solution

d. 2-week post-treatment stage: T25d ~ T39d

【Group 1-Facial Serum group】

A.M.: Standard cleanser + Test serum + Standard moisturizer + Standard Sunscreen

P.M.: Standard cleanser + Test serum + Standard moisturizer

【Group 2-Non-treatment group】

A.M.: Standard cleanser + Standard moisturizer + Standard Sunscreen
P.M.: Standard cleanser + Standard moisturizer

The standard sunscreen needs to apply to face every morning 15 minutes before sun exposure and re-apply if necessary. Keep out of eyes. No any other skin care or facial make up products are used.

7. Procedure

7.1. Screening

Participation of the volunteers is purely voluntary. Before being entered into the study, the volunteers will be pre-screened by the investigator according to the criteria indicated in the selection of volunteers' section. Only subjects who meet the requirements of this section are eligible to participate in the study.

7.2. Conducting the Study

Pre-screening visit at T-7d

a. Within 24 hours before screening visit, subjects will be asked not to use any cosmetic product on test areas.
b. On the arrival, the subject will be informed about the nature of the study and the treatment procedure and a signed and dated informed consent form will be obtained. At the same time, one Photo release form will be also signed from each subject.
c. A subject screening number will be automatically allocated (SC0X) by CRF.
d. Demographic data collection.
e. Medical examination, subject's interview on his medical history and concomitant medications.
f. Subjects wash face with usual cleanser, then pat dry with clean tissue paper at center.
g. Acclimatization to the room condition for 30 minutes (the conditions with a well-controlled room temperature (21± 1 °C) and humidity (45% ± 5 %).
h. Clinical assessment by will be done by dermatologist for screening.
i. Verification of subject eligibility: inclusion/non-inclusion criteria and on-site clinical grading by Dermatologist.
j. The weighted wash-out products and daily log will be delivered to each subject.
k. Adverse Events/Local Intolerance will be checked and recorded.

Evaluation visit on T0: Baseline

a. Subjects wash face with usual cleanser, then pat dry with clean tissue paper at center.
b. Acclimatization to the room condition for 30 minutes (the conditions with a well-controlled room temperature (21± 1 °C) and humidity (45% ± 5 %).
c. Verification of inclusion/non-inclusion criteria for final eligibility.
d. Clinical Assessment will be done by dermatologist for T0.
e. VISIA 7 will be done by trained technician for T0.
f. OCT scan will be done by trained technician for T0.
g. Corneometer will be done by trained technician for T0.
h. Vapometer will be done by trained technician for T0.
i. Cutometer will be done by trained technician for T0.
j. pH meter will be done by trained technician for T0.

k. LA sting test will be done by trained technician for T0.
l. The wash-out (standard) products will be weighted and returned to subjects; as the same time, the weighted investigational products and daily log will be delivered to each subject according to the randomization table.
m. Adverse Events/Local Intolerance will be checked and recorded.

T0 to T14d

a. Subjects should apply the provided wash-out products twice a day at home, in the morning and in the evening.

Evaluation visit on T14d

a. Subjects wash face with usual cleanser, then pat dry with clean tissue paper at center.
b. Acclimatization to the room condition for 30 minutes (the conditions with a well-controlled room temperature (21± 1 °C) and humidity (45% ± 5 %).
c. Clinical Assessment will be done by dermatologist for T14d.
d. VISIA 7 will be done by trained technician for T14d.
e. OCT scan will be done by trained technician for T14d.
f. Corneometer will be done by trained technician for T14d.
g. Vapometer will be done by trained technician for T14d.
h. Cutometer will be done by trained technician for T14d.
i. pH meter will be done by trained technician for T14d.
j. LA sting test will be done by trained technician for T14d.
k. Self-assessment questionnaire will be answered by subjects for T14d.
l. The investigational products and standard products will be weighted and returned to subjects, meanwhile, the daily log will be also checked.
m. Adverse Events/Local Intolerance will be checked and recorded

Chemical Procedure visit and Timme evaluation on T15d

a. Subjects wash face with usual cleanser, then pat dry with clean tissue paper at center.
b. One questionnaire should be answered by subjects.
c. Pre-process of xxx for procedure preparation.
d. CO_2-laser will be done by medical technologist.
e. Clinical Assessment will be done by dermatologist for Timm post-procedure.
f. VISIA 7 will be done by trained technician for Timm post-procedure
g. OCT scan will be done by trained technician for Timm post-procedure
h. Corneometer will be done by trained technician for Timm post-procedure
i. Vapometer will be done by trained technician for Timm post-procedure
j. Cutometer will be done by trained technician for Timm post-procedure
k. pH meter will be done by trained technician for Timm post-procedure
l. Adverse Events/Local Intolerance will be checked and recorded.

Evaluation visit on T16d (1-day after self-recovery)

a. Clinical Assessment will be done by dermatologist for T16d.
b. VISIA 7 will be done by trained technician for T16d.
c. OCT scan will be done by trained technician for T16d.

d. Corneometer will be done by trained technician for T16d.
e. Vapometer will be done by trained technician for T16d.
f. Cutometer will be done by trained technician for T16d.
g. pH meter will be done by trained technician for T16d.
h. Self-assessment questionnaire will be answered by subjects for T16d.
i. Adverse Events/Local Intolerance will be checked and recorded.

Evaluation visit on T18d (3-day after self-recovery)

a. Clinical Assessment will be done by dermatologist for T18d.
b. VISIA 7 will be done by trained technician for T18d.
c. OCT scan will be done by trained technician for T18d.
d. Corneometer will be done by trained technician for T18d.
e. Vapometer will be done by trained technician for T18d.
f. Cutometer will be done by trained technician for T18d.
g. pH meter will be done by trained technician for T18d.
h. Self-assessment questionnaire will be answered by subjects for T18d.
i. Adverse Events/Local Intolerance will be checked and recorded.

Evaluation visit on T22d (7-day after self-recovery)

a. Clinical Assessment will be done by dermatologist for T22d.
b. VISIA 7 will be done by trained technician for T22d.
c. OCT scan will be done by trained technician for T22d.
d. Corneometer will be done by trained technician for T22d.
e. Vapometer will be done by trained technician for T22d.
f. Cutometer will be done by trained technician for T22d.
g. pH meter will be done by trained technician for T22d.
h. Self-assessment questionnaire will be answered by subjects for T22d.
i. Adverse Events/Local Intolerance will be checked and recorded.

Evaluation visit on T25d (10-day after self-recovery and post-treatment started)

a. Subjects wash face with usual cleanser, then pat dry with clean tissue paper at center.
b. Acclimatization to the room condition for 30 minutes (the conditions with a well-controlled room temperature (21± 1 °C) and humidity (45% ± 5 %).
c. Clinical Assessment will be done by dermatologist for T25d.
d. VISIA 7 will be done by trained technician for T25d.
e. OCT scan will be done by trained technician for T25d.
f. Corneometer will be done by trained technician for T25d.
g. Vapometer will be done by trained technician for T25d.
h. Cutometer will be done by trained technician for T25d.
i. pH meter will be done by trained technician for T25d.
j. LA sting test will be done by trained technician for T25d.
k. Self-assessment questionnaire will be answered by subjects for T25d.
l. The investigational products and standard products will be weighted and returned to subjects, meanwhile, the daily log will be also checked.
m. Adverse Events/Local Intolerance will be checked and recorded.

Subjects will be pushed and required to answer one on-line questionnaire after the first application of test product at home.

Evaluation visit on T32d (7-day post-treatment started)

a. Subjects wash face with usual cleanser, then pat dry with clean tissue paper at center.
b. Acclimatization to the room condition for 30 minutes (the conditions with a well-controlled room temperature (21± 1 °C) and humidity (45% ± 5 %).
c. Clinical Assessment will be done by dermatologist for T32d.
d. VISIA 7 will be done by trained technician for T32d.
e. OCT scan will be done by trained technician for T32d.
f. Corneometer will be done by trained technician for T32d.
g. Vapometer will be done by trained technician for T32d.
h. Cutometer will be done by trained technician for T32d.
i. pH meter will be done by trained technician for T32d.
j. Self-assessment questionnaire will be answered by subjects for T32d.
k. The investigational products and standard products will be weighted and returned to subjects, meanwhile, the daily log will be also checked.
l. Adverse Events/Local Intolerance will be checked and recorded.

Evaluation visit on T39d (14-day post-treatment started)

a. Subjects wash face with usual cleanser, then pat dry with clean tissue paper at center.
b. Acclimatization to the room condition for 30 minutes (the conditions with a well-controlled room temperature (21± 1 °C) and humidity (45% ± 5 %).
c. Clinical Assessment will be done by dermatologist for T39d.
d. VISIA 7 will be done by trained technician for T39d.
e. OCT scan will be done by trained technician for T39d.
f. Corneometer will be done by trained technician for T39d.
g. Vapometer will be done by trained technician for T39d.
h. Cutometer will be done by trained technician for T39d.
i. pH meter will be done by trained technician for T39d.
j. LA sting test will be done by trained technician for T39d.
k. Self-assessment questionnaire will be answered by subjects for T39d.
l. The investigational products and standard products will be weighted and returned; meanwhile, the daily log will be also checked.
m. Adverse Events/Local Intolerance will be checked and recorded.

NB: all concomitant medications, AEs and local intolerances will be reported throughout the study.

8. Biostatistics and Data Management

8.1. Statistical considerations

All statistical tests will be two-sided and at the 5% level of significance.

8.2. Descriptive analysis

Descriptive statistics will be provided by one treatment group according to criteria nature:

- Quantitative: number of observed values (nobs), mean, standard deviation (SD), standard error (SE), median, 1st and 3rd quartiles (Q1:Q3), minimum and maximum.
- Qualitative: number of observed values (nobs), number (n) and percentage (%) of patients per class

The number of subjects by treatment group in the subject set (N) will be also given.

Descriptive statistics will be performed on per protocol population and will be provided for all demographic and baseline characteristics:

- ✓ Age
- ✓ Gender
- ✓ All attributes of Clinical Assessment Score
- ✓ Score of LA Sting Test
- ✓ Value of Instrumental Measurement Value
- ✓ Value of Imaging Analysis (OCT)

8.3. Efficacy Verification

8.3.1 Comparison between Time-points

A Shapiro-Wilk test will be used to test for normality of the baseline data (T0) and the change from baseline data (Tn-T0) at post-baseline time points at significance level alpha=0.01. When data passes normality (all normality of the distributions is confirmed for the same parameter), a parametric test will be used to test the null hypothesis that the mean change from baseline is zero. When data fails normality (if one or more normality of the distributions for the same parameter is rejected), a non-parametric test will be used.

Pre-treatment efficacy:

a) T14d (after pre-treatment), T15d (Timm post-procedure) versus T0 (baseline)
b) T16d (1-day after self-recovery), T18d (3-day after self-recovery), T22d (7-day after self-recovery), T25d (10-day after self-recovery) versus T15d (Timm post-procedure)

Post-treatment efficacy:

a) T32d (7-day after product treatment), T39d (14-day after product treatment) versus T25d (product treatment start)

The following will be calculated and reported for each evaluation parameter at applicable post-statistical baseline time point(s):

$$\text{Percent mean change from baseline} = \frac{(\text{Visit mean score} - \text{baseline mean score}) \times 100}{\text{baseline mean score}}$$

For self-assessment questionnaires, only the data of completing subjects will be analyzed. Questionnaire response options will be in the form of a 5-point semi-structured scale, ranging from one (1) to (5), where the score of one (1) will be the most negative/unfavorable rating and the score of five (5) will be the most positive/favorable rating the product can receive (the scale will also include a mid-point label "neither agree nor disagree"). Responses obtained for each question will be tested for normality using a Shapiro-Wilk test at significance level alpha=0.01, and if the data passes normality testing, mean scores will be used. Responses that are not normally distributed will be assessed using the median response. The percentage of ratings from

4 to 5 ("top XX box %") will be reported.

In the report appendices, raw data and open-ended questionnaire responses will be listed by subject. Data frequency and percentage will be presented for questionnaires and tolerability evaluations. Tolerability tables will also be sent to the Sponsor at the indicated interim data time points; SAQ data will be sent at study completion, for all completing subjects. Medians, means and percentage values will be reported to decimal place (0.0) for all questionnaire data.

A more appropriate analysis may be performed, which will be recorded in a Note to File and/or in the study report.

8.3.2 Comparison between Treatments

Paired T test for the same sample size or the independent T test for the different sample size will be used to identify the difference efficacy between treatments if the data fit normal distribution.

- ***Group 1****-Facial Serum group*
- ***Group 2****-Non-treatment control group*

Evaluation	Attributes	Comparison
Clinical Assessment	•**Skin symptoms scoring post-procedure:** - Dryness - Erythema - Papules - Desquamation - Chromatosis - Edema - Escharosis •**Skin qualities:** - Skin elasticity - Skin evenness - Skin brightness - Skin smoothness - Skin radiance - Appearance of pores on cheek - Crow's feet wrinkle - Epithelial cell confluence - Over healthy appearance	Group 1 versus Group 2
Instrumental Assessment	Skin hydration by Corneometer Transepidermal water loss (TEWL) by Vapometer Skin elasticity by Cutometer Skin pH by Skin-pH-Meter	
Imaging Analysis	Attributes output from VISIA 7 Attributes output from OCT (The thickness of epidermis)	
LA stinging Test	•**Skin symptoms scoring:** - Stinging - Itching - Burning	
Tolerance Feedback	•**Skin symptoms scoring:** - Area - Severity - Start time - During time	

9. Further Study Documentation

9.1. Protocol Amendment

Any protocol amendment (Annex 11.5) signed by mutual agreement is documented.

9.2. Dropouts

Subjects may withdraw from the study at any time. In the case of withdrawal, the reason of withdrawing is documented and reported.

9.3. Deviations from Protocol

Protocol deviations (Annex 11.6) are documented and reported.

9.4. Adverse Event Reporting

Unexpected or unusual medical events or clinical symptoms are documented in an adverse event form (Annex 11.7). The subjects are instructed to immediately contact the test site to be examined by the investigator and/or designee. If this event is a medical condition that is not part of the subject's medical history, it is documented.

The investigator or designee will notify the sponsor representative of any adverse events (within 24 hours) or any severe adverse events (immediately) or any events that are related to study participation.

10. Ethical Considerations

According to this study (protocol, ICD/Assent Document, and all addenda) will be reviewed and approved by an Ethic contacted by the Study Site.

Details of the Ethic for this study are indicated below:

- Name: Independent Ethics Committee, Shanghai Clinical Research Center
- Address: Building 10, No 140 Tianlin Road, Shanghai, 200233 200032, P. R. China
- Contact details: +86-21-33676540, hongxia.zhang@scrcnet.org

It is the responsibility of the PI to have Ethic approval of the study protocol, protocol amendments, ICD/Assent Document(s), and other relevant documents, e.g., advertisements, as applicable.

The study will not be activated and subjects will not be recruited, consented, or receive study materials until such time as the Ethic has approved the required documentation. In addition, the Ethic will review the study before any significant change in the protocol is initiated. After each review, the Ethic's approval letter will be forwarded to the Sponsor. All correspondence with the Ethic should be retained in the study master file to storage.

11. Annex

11.1 Subject Eligibility Check List

11.2 Hyperpigmentation Skin Questionnaire

11.3 Self-assessment Questionnaire

11.4 DIARIES for Tolerance Feedback in Daily

11.5 Protocol Amendment Document

11.6 Protocol Deviation Record

11.7 Adverse Event Report Form

Annex 11.1. Subject Eligibility Check List

Test No.: Volunteer No.:	Sex: ☐ female ☐ male	Age:

1.	Chinese women, 20-50 years old;	☐	yes	☐	no
2.	All skin types (dry, normal, oily and mixed)；	☐	yes	☐	no
3.	Rough ad dull skin by self-declared；	☐	yes	☐	no
4.	Lack of radiance, brightness, smoothness by self-claimed;	☐	yes	☐	no
5.	Presenting with problems of acne mark, acne scar or blemishes on face;	☐	yes	☐	no
6.	Did not participate any clinical test or cosmetic product test on skin within 3 months;				
7.	Did not participate any chemical procedures for previous 2 months; and willing to not participate any procedures during the whole study;				
8.	Did not participate any clinical test or cosmetic product test on skin within 3 months；				
9.	No disagreement of dermatologist because of other reasons that exclude the participation of the volunteer.	☐	yes	☐	no
10.	In general good health at the time of the study.				
11.	Willing and able to participate as evidenced by signing of informed consent?				
12.	Must be willing to comply with all study protocol requirements.				
13.	Are you in general good health at the time of study?	☐	yes	☐	no
14.	Are you willing and able to participate as evidenced by signing of informed consent?	☐	yes	☐	no
15.	Are you intending to get pregnant, in pregnancy, lactation or the periodof 6 months after childbirth?	☐	yes	☐	no
16.	Do you take part in another study, which is carried out on the same skin area?	☐	yes	☐	no
17.	Do you have known allergies against skin / hair care product or topical medicine or alcohol?	☐	yes	☐	no
18.	Do you have any other serious illness or diseases?	☐	yes	☐	no
19.	I have read theen closed "Information forVolunteers" with fully understanding.	☐	yes	☐	no
20.	The possibility of adverse reactions occurred by applying products has been sufficiently and scientifically foreseen. Your safety will be ensured to the best of our ability. But during the study or the latter part of the study, there may be the adverse reactions caused by force majeure, which will be confirmed by professional medical institutes. Do you fully understand and agree with it?	☐	yes	☐	no
21.	I have been fully informed about the implement, execution and risks involved in the study. I voluntarily take part in this study; my data can be anonymously passed to relevant departments, institutes or firms. Details about this study are volunteer to secrecy. I'm not allowed to pass them to anyone.	☐	yes	☐	no
22.	Your name or other personal information will not be overt. Your data can be anonymously passed to relevant government departments, other institutes or firms. If the facial image capture is taken in the project and the results are published on other academic purposes, and your facial images need to use, we will also take measures (for example, add a black bar to cover the image of the eyes) so as to fully guarantee that you will not be identified. Do you fully understand and agree with it?	☐	yes	☐	no
23.	I have read and understood all above asked questions and answered them truth fully.	☐	yes	☐	no

Signature of Volunteer: ..... Date: .....
Responsible Tester: ..... Date: .....

Annex 11.2. Hyperpigmentation Skin Questionnaire

Hyperpigmentation Skin Questionnaire

色素沉着性皮肤问卷

Q1. When having acne, dark brown/ black marks usually left on skin surface:
长过痘痘后的部位会留下深棕色/黑色的印记：

A. Never
从不
B. Sometimes
有时会
C. Often
经常会
D. Always
总是这样
E. Never having acne
我从没长过痘痘

Q2. When having skin scratch, the brown marks usually last:
被割伤后，棕色的印记（不是新愈合时粉色的疤）会残留多久：

A. None marks
不会留下疤痕
B. 1 week
1 周
C. Several weeks
几周
D. Several months
好几个月

Q3. Taking oral contraceptive pills or other hormone replacement or in duration of pregnancy, dark spots usually appear:
当你怀孕、服用口服避孕药丸或其他荷尔蒙替代类药物时，脸上会长出深色斑点：

A. None spot
没有斑点
B. One spot
1 个
C. A few spots
少量
D. Many spots

很多

Q4. Dark spots/patches on your upper lip or cheeks:
你的上唇或面颊有深色斑点/块吗？

A. None
没有
B. Not sure
我不确定
C. Yes，slightly
是的，一点明显
D. Yes，obviously
是的，非常明显

Q5. Sunburn gets worse after skin exposure in the sun：
日晒之后斑点会加深：

A. None sunburn
我没有深色斑点
B. Not sure
无法确定
C. A little
有点加深
D. Much worse
变深很多
E. Never having skin exposure in the sun
我从不直接接触阳光

Q6. Your facial skin has been diagnosed with pigmentation or light/dark brown/gray spots:
你的面部皮肤曾经被诊断为有色素沉积、或有浅/深棕/灰色斑：

A. Never
没有
B. Once
有一次
C. Yes, but it disappeared.
是的，但是后来消失了
D. Yes, but it never disappeared.
是的，仍然存在
E. Not sure
无法确定

Q7. Having or ever had small brown spots (freckles or sunburn) on the face, chest, back or arms:
脸部、前胸、后背或手臂是否有或者曾经有小的棕色斑点（雀斑或晒斑）：

A. None
没有
B. Several（1-5 spots）
有一些（1-5 个）
C. Some（6-15 spots）
有很多（6-15 个）
D. Many（more than 16 spots）
非常多（16 个以上）

Q8. First time skin exposure in the sun in several months (e.g., early spring or summer), your skin feels:
几个月来第一次晒太阳（例如刚入春或入夏），皮肤感觉：

A. Burning
灼热
B. Burning and dark marks appear thereafter
灼热然后变黑
C. Dark marks appear immediately
直接变黑
D. Not sure. I have dark skin.
我也分不清，我的肤色已经很深了

Q9. Skin exposure in the sun for several days:
连续数天暴露于阳光下：

A. Burning and blister, but it doesn't affect my skin tone.
灼热甚至起泡，但我的肤色没有什么变化
B. Skin tone gets slightly darker
肤色变深了一点
C. Skin tone gets much darker
肤色变深了很多
D. Not sure. I have dark skin.
我也分不清，我的肤色已经很深了

Q10. Insolation leads freckle appearance:
日晒有没有引起雀斑

A. Never
我从没长过雀斑
B. Sometime
偶尔长出一些
C. Often
经常长出一些
D. Not sure. I have dark skin.
我也分不清，我的肤色已经很深了

Q11. If any of your family member has freckle on face, please describe the severity:
你的父母中有人长雀斑吗？如果有，请描述程度。

A. None
没有
B. Some
有一些
C. Many
有很多
D. Many on face, chest, back, neck and shoulders
脸上、前胸、后背、颈脖肩膀都有很多
E. Not sure
不确定

Q12. Your nature hair color:
你的天然发色是：

A. Red
红色
B. Black
黑色
C. Brown
棕色
D. Blond
金色

Q13. The history of melanoma among family members:
家庭的直系亲属中是否有黑素瘤病史：

A. None
没有
B. Only one family member
有一个人
C. More than one family member
一人以上
D. I have a history of melanoma.
我自己有黑素瘤病史
E. Not sure
不确定

Scoring criteria:
评分：
A: 0p B: 1p C:2p D:3p E: 1p
A: 0 分 B: 1 分 C:2 分 D:3 分 E: 1 分

≤ 14p Low risk of pigmentation inducement
低色素沉着风险
15p-27p Medium risk of pigmentation inducement

	中色素沉着风险
28p-44p	High risk of pigmentation inducement 高色素沉着风险

Annex 11.3. Self-assessment Questionnaire

Answers given according to a 5-point scale："5-completely agree 非常同意", "4-somewhat agree 比较同意" "3-neither agree 说不上同意不同意", "2-somewhat disagree 比较不同意", "1-completely disagree 非常不同意"

Self-assessment - Pre-treatment **术前 14 天产品使用问卷**	**Yes/是**	**No/否**	**Comments/ 其他**
I feel skin is good prepared for procedure **我觉得我的肌肤更强韧了，为特殊美容做好了准备**			
I feel skin is comfort for procedure **我觉得我的皮肤在特殊美容中更耐受了**			
Skin feels intensively repaired **肌肤感觉被深层修护**			
I feel skin redness due to dryness is less occur? **我感觉皮肤由于干燥而发红的情况减少了**			
Skin feels strengthened **肌肤感觉更强韧**			
Skin feels hydrated **肌肤感觉水润保湿**			
Skin feels comfortable **肌肤感觉舒服**			
Skin feels smoother **肌肤感觉更光滑**			
Skin looks brighter **肌肤看起来更明亮**			
Skin looks more radiant **肌肤看起来更有光泽**			
Pores look less visible **毛孔看起来不明显**			
Skin feels more elastic **肌肤感觉更有弹性**			
Fine line looks less visible **细纹看起来不明显**			
Crow's feet wrinkle is reduced **鱼尾纹看上去减少了**			
Self-assessment – Recovery **术前后 1 天，3 天，7 天，10 天恢复期问卷**			
I feel pre-treatment with product help my skin recover fast after procedure **我感觉提前 14 天使用产品，可以帮助肌肤在特殊美容后更快修复**			
I feel pre-treatment with product help my skin recover			

stable after procedure **我感觉提前 14 天使用产品，可以帮助肌肤在特殊美容后更稳定**			
I feel pre-treatment with product help my skin recover comfortable after procedure **我感觉提前 14 天使用产品，可以帮助肌肤在特殊美容后更舒适**			
I feel pre-treatment with product help my skin redness recovered **我感觉提前 14 天使用产品，可以帮助肌肤在特殊美容后褪红**			
I feel pre-treatmet with product help my skin dryness recovered **我感觉提前 14 天使用产品，可以帮助肌肤在特殊美容后降低干燥爆皮**			
I feel pre-treatment with product help my skin discomfort (e.g. red/dry/itch) from procedure recovered faster **我感觉提前 14 天使用产品，可以使肌肤在特殊美容后的不适症状（如发红/干燥/瘙痒等）更快修复**			
I would like to recommend my friends to use product before procedure **我很乐意推荐我的朋友们，在特殊美容前使用产品**			
I feel skin is comfort for procedure **我觉得我的皮肤在特殊美容中更耐受了**			
Self-assessment **- Post-treatment** **术前 7 天及 14 天产品使用问卷**			
Post-treat with product after skin recovered, skin feels smoother **当肌肤在特殊美容恢复后，使用产品，肌肤感觉更光滑了**			
Post-treat with product after skin recovered, skin feels brighter **当肌肤在特殊美容恢复后，使用产品，肌肤感觉更明亮了**			
Post-treat with product after skin recovered, skin feels more radiant **当肌肤在特殊美容恢复后，使用产品，肌肤感觉更有光泽了**			
Post-treat with product after skin recovered, skin pore is less visible **当肌肤在特殊美容恢复后，使用产品，毛孔看起来不明显了**			
Post-treat with product after skin recovered, skin feels more elastic **当肌肤在特殊美容恢复后，使用产品，肌肤感觉更有弹性**			

Post-treat with product after skin recovered, fine line looks less visible **当肌肤在特殊美容恢复后，使用产品，细纹看起来不明显了**			
Post-treat with product after skin recovered, crow's feet wrinkle is reduced **当肌肤在特殊美容恢复后，使用产品，鱼尾纹看起来不明显了**			
Post-treat with product after skin recovered, skin feels intensively repaired **当肌肤在特殊美容恢复后，使用产品，肌肤感觉被深层修复**			
Post-treat with product after skin recovered, skin feels strengthened **当肌肤在特殊美容恢复后，使用产品，肌肤感觉更强韧了**			
Post-treat with product after skin recovered, skin feels hydrated **当肌肤在特殊美容恢复后，使用产品，肌肤感觉水润保湿**			
Post-treat with product after skin recovered, skin feels comfortable **当肌肤在特殊美容恢复后，使用产品，肌肤感觉舒适**			
I would like to recommend my friends to use product for post-treat **我很乐意推荐我的朋友们，在特殊美容后使用产品**			

Annex 11.4. DIARIES for Tolerance Feedback in Daily

RD Number：_____ **Subject Initial：_____**

No. 序号	Treatment 产品	Date(Y/M/D) 日期（年/月/日） 使用后填写		Without Irritation (√) 未发生任何不良的情况 (请打钩)	Skin Irritation 皮肤有反应时填写				
					Symptom 出现的症状	Area 症状发生的部位	Severity 症状的程度	Start Time 症状开始时间	During Time 症状持续时间
					1. Redness 发红 2. Dryness 干燥 3. Stinging 刺痛 4. Itching 瘙痒 5. Tightening 紧绷感 6. Burning 发热/灼烧感 7. Others(specific) 其他 (请注明)	出现的症状在哪些部位? 1. Eye 眼部 2. Forehead 额头 3. Cheek 脸颊 4. Lip corner 嘴角 5. Chin 下巴 6. Others(specific) 其他 （请注明）	1. Very slight 非常轻微 2. Slight 轻微 3. Moderate 中度 4. Extensive 重度 5. Very severe 非常严重	使用产品后多长时间皮肤开始有反应? 1. Immediate 用后立即 2. 30mins after using 用后 30 分钟内 3. 30mins to several hours after using 用后 30 分钟至几个小时 4. Several days after using 用后____天	How long is the irritation lasting? 皮肤反应的特征持续了多长时间?
D1			早						
			晚						
D2			早						
			晚						
D3			早						
			晚						
D4			早						
			晚						
D5			早						
			晚						
D6			早						
			晚						
D7			早						
			晚						
D8			早						
			晚						
D9			早						
			晚						
D10			早						
			晚						
D11			早						
			晚						
D12			早						
			晚						
D13			早						
			晚						
D14			早						
			晚						
D15~D56			早						
			晚						

Annex 11.5. Protocol Amendment Document

Sponsor:		**Implementation:**	

Project Title:		**Project No.:**	
Contract No.:		**Protocol Edition:**	
Amendment Date:		**Valid Date:**	
Amendment content: **Original Item:** **Amendment Item：** **Reason:**			

By mutual agreement, both parties signed this protocol amendment document.

Sponsor Signature/Date： **Implementation Signature/Date：**

Annex 11.6. Protocol Deviation Record

Page ____ of _____

IF THERE IS NO DEVIATIONS OCCURRED DURING THE STUDY, PLEASE SIGN IN BELOW.

Investigator_Date_____

IF THERE IS ANY DEVIATION, PLEASE FILL IN THE FOLLOWING SECTION

Date: **Explanation of Deviation and Action**

_____ _____
_____
_____

_____
Investigator

Date: **Explanation of Deviation and Action**

_____ _____
_____
_____

_____
Investigator

Date: **Explanation of Deviation and Action**

_____ _____
_____
_____

_____
Investigator

Date: **Explanation of Deviation and Action**

_____ _____
_____
_____

_____
Investigator

Annex 11.7. Adverse Event Report Form

CN-CLI-21-14049-46	Adverse Event Management	Application Date:

Adverse Event Form

Information of Subjects 受试者信息	Name 姓名： Age 年龄： Gender 性别： Contact No.电话： Previous Allergies 既往过敏史：
Test Information 测试信息	Description of test design 所参加测试的描述：
Product Information 产品信息	Name 配方全名： Fla. No.配方号： Batch N°
Nature of AE 性质 Use the specific and concise terms. Please indicate the signs and symptoms. For the cutaneous adverse events, please indicate the location. 请使用简明的言语并描述病症 皮肤相关的不良事件请注明部位	
Start date 开始日期	(YYYY/MM/DD)
Duration 持续时间	____ Days____ hour____ min
Ending date 结束日期	(YYYY/MM/DD) or □ In progress 进行中
Intensity 强度	☐ Slight 轻度 ☐ Moderate 中度 ☐ Severe 重度
Time between last application and beginning of reaction **反应出现前最后一次使用产品与反应出现的时间间隔**	____ Days____ hour____ min
How long have you been using this product prior to this reaction? **反应出现前，此产品总共使用了多久**	
With which frequency? **使用次产品的频率**	
Area product applied: **使用部位**	
Other products used simultaneously in same area: **相同部位同时使用的其他产品**	

CN-CLI-21-14049-46_A1V1 Adverse Event Form

-Confidential-

CN-CLI-21-14049-46	Adverse Event Management	Application Date:

Action undertaken on the investigational product **对本测试产品采取的措施**	☐ None 无 ☐ Temporary halt 暂停后又恢复 ☐ Early termination 停止使用 ☐ Adjustment of the posology (explain in the comments) 调整剂量（备注中详述）
Medical Consultation: **治疗**	Name of the Doctor: 医生姓名 Name of the Hospital: 医院名 Diagnosis： 诊断 Patch Test: Yes 是□ No 否□ 是否做斑贴试验 Result of Patch Test: 斑贴试验结果
Follow up 事件后续	☐ Resolved 症状小时 ☐ Persistent 症状持续 ☐ Death 死亡 ☐ Unknown 不详
SAE 严重不良事件	☐ Yes 是 □ No 否
Relation to the investigational product **和本测试产品的关系**	☐ None 肯定无关 ☐ Little probable 基本无关 ☐ Possible 可能有关 ☐ Probable 很可能有关 ☐ Sure 肯定有关
Investigator's Name **研究人员姓名** **Date** **日期** **Signature** **研究人员签名**	

CN-CLI-21-14049-46_A1V1 Adverse Event Form

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