An 8-week full face HUT design, single center, double blinded, controlled and randomized study to evaluate different product regimens' performance on protecting skin with resilience under tracked city environmental aggressors

Study Number	**CS-2017-14/ CO-170223145432-SACT**
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Study Location	**Shanghai Skin Disease Hospital** **1278 Baode Road** **Shanghai, People's Republic of China**
Principal Investigator	**Chao Yuan, M.D., PhD** **dermayuan@163.com**
Study Start Date	**2017-05-18**
Study Complete Date	**2017-07-25**
Report Version & Date	**1.0 / 2018-02-26**

1. STUDY TEAM AND SITE

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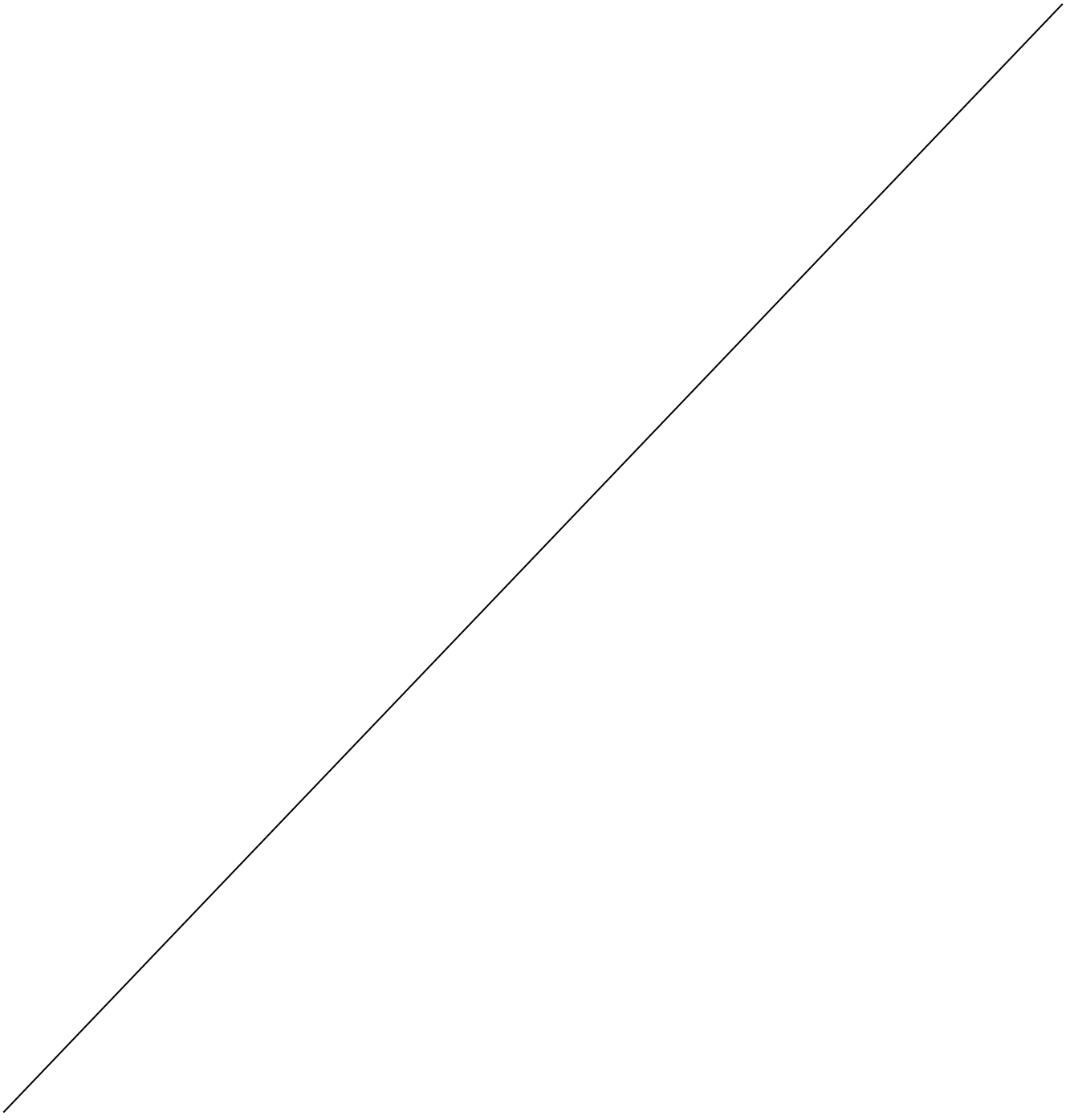
2. LIST OF ABBREVIATIONS

Abbreviation	Definition
-3D	Screening visit
BL	Baseline
AA	2-4hours after product application
3H	3hours after product application
8H	8hours after product application
1W	1 week after baseline
4W	4 weeks after baseline
8W	8 weeks after baseline
8W+3D	8 weeks + 3 days after baseline
a.u.	Arbitrary Unit
AE	Adverse Event
ANOVA	Analysis of Variance
DPR	Designated Physician Representative
GATT	Global Activity Tracking Tool
HUT	Home Use Test
ICH GCP	International Council for Harmonisation Good Clinical Practice
ICD	Informed Consent Document
ID	Identification
IEC	Independent Ethics Committee
IP	Investigational Product
IRB	Institutional Review Board
LSD	Least Significant Difference
Max	Maximum
Min	Minimum
MMD	MoistureMeter-D
NT	No-treatment
NTG	Neutrogena
No.	Number
PI	Principal Investigator
PM	Particulate Matter
PQC	Product Quality Complaint
QoL	Quality of Life
QN	Questionnaire
RH	Relative Humidity
SAE	Serious Adverse Event
SC	Stratum Corneum
SD	Standard Deviation/Study Director
Sec	Second

Abbreviation	**Definition**
SM	Study Manager
SMF	Site Master File
SPSS	Statistical Product and Service Solutions
SSDH	Shanghai Skin Disease Hospital
TEWL	Transepidermal Water Loss
TMF	Trial Master File
UV	Ultraviolet
VC98	Visioscan VC98



3. STUDY REPORT SYNOPSIS

PROTOCOL TITLE	An 8-week full face HUT design, single center, double blinded, controlled and randomized study to evaluate different product regimens' performance on protecting skin with resilience under tracked city environmental aggressors
PROTOCOL IDENTIFICATION	CO-170223145432-SACT (GATT No.) NTG-01-2017-02 (AP Skin Testing Center No.) CS-2017-14 (Site study No.)
OBJECTIVE(S)	1. To investigate the product regimens' performance on moisturization related skin healthy signs (skin moisturization, barrier function, elasticity, translucency, roughness and overall skin conditions) through instrumental evaluation, clinical grading and self-assessment before, during and after 8 weeks' home usage under city environmental aggressors (Sun, change of temperature and humidity, wind and air pollution) among 3 product regimens and Non-treatment control; 2. To investigate product regimens' tolerance and safety via Home Use Test; 3. To explore the linkage among products efficacy, ambient aggressors and life habits (data will be analyzed and reported separately); 4. To collect skin microflora/microbiome samples for potential research on skin microbiome distribution change as impacted by product application and/or environmental aggressors change (data will be analyzed and reported separately).
STUDY DESIGN	Single center, double blinded, controlled and randomized 8-week home use clinical trial.
STUDY POPULATION	Healthy Chinese female subjects from 18 to 40 years of age who met the eligibility criteria.
SAMPLE SIZE	The site enrolled 122 subjects, from which 110 subjects completed the study divided by 38 (L), 35 (C) and 37 (K) per group. Sample size of minimum 35 volunteers per group had been considered sufficient per group. Subjects were randomly divided into 3 groups with different facial care regimens during the 8-week home use study. **Group 1:** NTG Hydro Boost Gelee Milk Cleanser + NTG Hydro Boost Kiwi Water Gel **Group 2:** NTG Hydro Boost Gelee Milk Cleanser + NTG Hydro Boost Water Gel **Group 3:** NTG Hydro Boost Gelee Milk Cleanser + NTG Hydro Boost Extra Dry Emulsion
INVESTIGATIONAL STUDY MATERIALS	

Product Name	Product Type	Formula No.	Product Code	Batch No.	Remark
NTG Hydro Boost	Facial Gel Cream	12858-044	C	B161023A	Marketed product

	Water Gel					
	NTG Hydro Boost Kiwi Water Gel	Facial Gel Cream	11476-154	K	NEMOG170417/A, NEMOG170417/B	Non-marketed product
	NTG Hydro Boost Extra Dry Emulsion	Facial Gel Cream	12858-038	L	B161231A1	Marketed product
	NTG Hydro Boost Gelee Milk Cleanser	Facial Cleanser	SQ086-29248	U	001 20160713	Marketed product
DOSE AND MODE OF APPLICATION	After the subject's enrollment, no product could be applied on the face and upper chest but only water washes (face wash twice per day in the morning and evening, together with upper chest wash for 3 days (wash-in period) including the night before baseline (BL) measurement. After baseline (BL) measurement, the product regimens were applied onto face under site instruction according to the randomization form. Measurements were taken at 2-4 hours and 8 hours after product regimens' application. Upper chest area was measured as no treatment (NT) control. Then one product regimen included a facial cleanser and a facial cream was randomly distributed to each subject for 8-week home usage by following the same use instruction as on-site application. Both cleanser and cream products were applied twice a day in the morning and evening on whole face. For the upper chest area, used water wash twice per day in the morning and evening, no any other product was allowed. After the 8-week home use of the assigned product regimens, subjects stopped using the products for 3 days (regression period). Subjects used water only to wash the face and upper chest twice per day in the morning and evening during the period.					

	Subjects were not allowed to use any other cosmetic products or topical treatment on face and upper chest except for the assigned products during the whole study period.
STUDY DURATION	For each subject, the study consisted of 6 visits over 9 weeks including visits at Screening (-3D), Baseline (BL), 1-week (1W), 4-week (4W), 8-week (8W) and 8-week+3days (+3D). The field work lasted from May 18, 2017 to Jul 25, 2017.
METHODOLOGY	1. Corneometer – Gives an estimation of moisture content of the skin surface via capacitance measurements; 2. MoistureMeter-D – To evaluate skin moisture content via skin dielectric constant measurements; 3. Tewameter – Evaluate skin barrier function by measuring Transepidermal Water Loss (TEWL) of the skin; 4. Cutometer – Measures elasticity of the upper skin layer; 5. Visioscan VC98 –Takes magnified images of the skin; 6. Translucency Meter – To investigate degree of translucency of skin; 7. VISIA-CR® (Canfield, US) –Digital imaging system to visualize skin features; 8. Air Radio A2SE – An electronic portable device (environmental tracker) to measure individual temperature, humidity and air quality (PM2.5/PM10) for further exploratory study; 9. Clinical grading; 10. Subject self-assessment Questionnaire (QN) on product performance; 11. Quality of Life Questionnaire (QoL); 12. Skin microbiome sampling for further exploratory study.
MEASUREMENT AND/OR EVALUATION SCHEDULE AND ASSOCIATED SUCCESS CRITERIA	Measurement Schedule: Subjects were required to visit the site at Screening (-3D), Baseline (BL), 1-week (1W), 4-week (4W), 8-week (8W) and 8-week+3days (+3D) for measurements. At baseline visit, measurements were taken at baseline (BL), 2-4 hours (AA) and 8 hours (8H) after product application
SAFETY AND ADVERSE EVENTS	There were no reports of any AE/SAE and pregnancy during this study. Products were well tolerated during the study period based on dermatological evaluation.
STATISTICAL METHODS	The statistical analysis was performed by the certified or trained statistician or his/her designee by using SPSS (IBM®). **Descriptive statistics:** • Demographic description

	• Mean (Max, Min)
	• Standard Deviation (SD)
	• Clinical grading: SUM (Median), Percentage (%) of improved subjects (from Baseline)
	• QN+ QoL: SUM (Median), TOP 2 box %
	• Safety and Tolerance: Score frequencies
	
	Hypothesis test:
	1. Within group multi-comparison (between time points):
	  • Comparisons between each time points and BL
	2. Between treatments (baseline adjusted):
	  • Non-treatment vs. product regimen (within each group)
	  • Comparisons among the 3 product regimens

EFFICACY CONCLUSIONS	All the products efficacy attributes were detected under the environmental challenge (Heat, Humidity, PM2.5, UV and Wind) from May to July in Shanghai during which the no-treatment site on upper chest showed trend of increased TEWL and skin surface moisture content, reduced skin elasticity and scaliness. **Skin Moisture:** All products had significantly improved skin surface moisture content at all time points since the 1st week after product application vs. BL, along the environmental challenges, showed skin resilience even 3 days after stop usage. All products had significantly improved skin surface moisture content comparing with NT at 3H and 8H, which indicated long lasting moisture benefits in a controlled environment. No significant difference between products at all time points except K improved more than C at 1W. **Skin Barrier Function:** All products had significantly improved relative skin barrier function (T/C ratio) at all time points (8H, 1W, 4W, 8W and 8W+3D) after product application vs. BL. The results indicated all regimen groups had long lasting relative skin barrier (T/C ratio) protection benefits in a controlled environment and defense along the environmental challenges to improve skin intrinsic relative barrier function, showed skin resilience even 3 days after stop usage. Significant improvement of relative skin barrier function (T/C ratio) was observed vs. NT since 1W till 8W+3D in all groups. Product L and C also showed significantly better improvement vs. NT at 8H.

	L improved more than K at 8H and C at 8H, 4W (TC ratio), which indicated L regimen group's superiority in long lasting protection and intrinsic skin barrier improvement than other groups. **Skin Translucency:** All 3 groups showed skin visible hydration/translucency improvement during and after stopping treatment. L showed improvement on translucency compare with NT at 1W, 4W and even after 3 days stopping usage. C showed improvement on translucency compare with NT at 4W, 8W and even after 3 days stopping usage. C showed selectively superiority than L and K at 8W and +3D. **Skin Scaliness (SEsc):** Scaliness significantly decreased for all products even 3 days after stopping usage. K, C showed benefits on reducing scaliness at some timepoints vs. no treatment. No significant differences detected between products **Skin Elasticity:** K showed elasticity benefit at 3H, 8H and 4H. L showed better elasticity at 8H. K showed better performance than L at 8W. **Clinical grading:** All clinical graded parameters showed an improvement trend for the 3 groups, though only selective time points with significant score decreases comparing with BL. Overall skin radiance significantly improved in all groups at W8, and C, K groups even lasted after stopping use for 3 days. All group show improved moisture vs NT，C has superiority vs K, L at 8w+3D. C showed benefits of improving Translucency vs. NT and K at 1W, 4W and 8W+3D.

4. STUDY REPORT SYNOPSIS SIGNATURE PAGE (EXTRACTED FROM FULL REPORT)

Clinical Study Report Approval Form

Protocol Title: An 8-week full face HUT design, single center, double blinded, controlled and randomized study to evaluate different product regimens' performance on protecting skin with resilience under tracked city environmental aggressors	
Project Name: HydroBoost 2.0/3.0	
Study ID	**Protocol Version Date**
CO-17170223145432-SACT (GATT No.) NTG-01-2017-02 (AP Skin Testing Center No.) CS-2017-14 (Site study No.)	Protocol: 21 April, 2017, Final Version 2.0 Protocol amendment: 19 May, 2017, Version 1.0

Investigational Products

Investigational Product (s)	Formula #	Batch #	Product Type
NTG Hydro Boost Water Gel	12858-044	B161023A	Facial Cream
NTG Hydro Boost Kiwi Water Gel	11476-154	NEMOG170417/ A, NEMOG170417/ B	Facial Cream
NTG Hydro Boost Extra Dry Emulsion	12858-038	B161231A1	Facial Cream
NTG Hydro Boost Gelee Milk Cleanser	SQ086-29248	001 20160713	Facial Cleanser

This clinical study report has been reviewed and approved by:

Name	Signature
Study Director *Fanqi Kong*	Fanqi Kong 数字签名者：Fanqi Kong DN：c=US, o=JNJ, ou=Subscribers, cn=Fanqi Kong, 0.9.2342.19200300.100.1.1=89412148 原因：I have reviewed this document. 日期：2018.03.21 10:18:46 +08'00' Adobe Acrobat 版本：11.0.10
Department Head *Cecilia Li*	Xi Li Digitally signed by Xi Li DN: c=US, o=JNJ, ou=Subscribers, cn=Xi Li, 0.9.2342.19200300.100.1.1=89407183 Reason: I have reviewed this document. Date: 2018.03.21 11:23:30 +08'00' Adobe Acrobat version: 11.0.10

11. REPORT SIGNATURE PAGE

Report prepared by:

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Principal Investigator Dr. Chao Yuan	Chao Yuan 2018/03/01
Sponsor Study Manager Yuanyuan Duan	Yuanyuan Duan Digitally signed by Yuanyuan Duan DN: c=US, o=JNJ, ou=Subscribers, cn=Yuanyuan Duan, 0.9.2342.19200300.100.1.1=89408281 Reason: I am the author of this document Date: 2018.02.27 13:45:18 +08'00'

Report reviewed by:

Role	**Signature and Date**
Sub-Investigator & Statistician Yafei Xu	Yafei Xu. 2018/03/01.
Quality Supervision Ying Cheng	Ying Cheng 2018/03/01.
Consultant Prof. Philippe HUMBERT	2018/03/19