

**PRO 2020-06**

**Clinical evaluation of CeraVe® Hydrating Cleanser and Moisturizing Cream for the improvement of skin condition in patients with diabetes mellitus related skin changes**

**Original Protocol**

**Investigator-Initiated Trial**

**NCT#04724967**

**Sponsor and Principal  
Investigator (PI):  
Sponsor/PI Address**

Robert S. Kirsner, MD PhD FRCPC

University of Miami  
Dr. Phillip Frost Dept. of Dermatology and Cutaneous Surgery  
1295 NW 14th St K-M  
Miami, FL  
33136, United States

**Date:**

24 July 2020

**Confidentiality Statement**

This document contains confidential information belonging to Robert S. Kirsner that must not be disclosed to anyone other than the recipient study staff and members of the independent ethics committee, institutional review board, or authorized regulatory agencies. This information cannot be used for any purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of Robert S. Kirsner.

**SIGNATURE PAGE**

**PROTOCOL NUMBER:** PRO-2020-06  
**PROTOCOL VERSION:** 6.0  
**PROTOCOL DATE:** 24 July 2020  
**PROTOCOL TITLE:** Clinical evaluation of the *CeraVe*® Hydrating Cleanser and Moisturizing Cream for the improvement of skin condition in patients with diabetes mellitus

Signatures of the below individual indicates that all agree this version is final:

---

Robert S. Kirsner

**Sponsor/Principle Investigator**

---

Date

# 1 TABLE OF CONTENTS

<b>SIGNATURE PAGE .....</b>	<b>2</b>
<b>1 TABLE OF CONTENTS .....</b>	<b>3</b>
<b>LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS .....</b>	<b>5</b>
<b>2 INTRODUCTION.....</b>	<b>6</b>
<b>3 STUDY OBJECTIVES.....</b>	<b>6</b>
<b>4 INVESTIGATIONAL PLAN .....</b>	<b>6</b>
4.1 Overall Study Design.....	6
4.2 Number of Study Centers .....	7
4.3 Duration of Participation .....	7
4.4 Duration of Study .....	7
4.5 Sample size .....	7
4.6 Inclusion Criteria .....	7
4.7 Exclusion Criteria .....	7
4.8 Analysis Populations .....	7
4.9 Primary Endpoint.....	8
4.10 Beginning and End of Study.....	8
4.11 Subject Withdrawal Criteria .....	8
4.11.1 Replacement of Subjects.....	9
4.12 Treatments .....	9
4.12.1 Dosage and Formulations .....	9
4.12.2 Method of Packaging, Labeling, Storage, and Dispensing .....	9
4.12.3 Study Product Accountability .....	9
4.12.4 Prior and Concomitant Medications .....	9
4.12.5 Assessment of Compliance .....	10
4.13 Study Procedures .....	10
4.13.1 Written Informed Consent .....	11
4.13.2 Significant Medical History/Demographic Information.....	11
4.13.3 Adverse Events and Serious Adverse Events Assessment .....	11
4.13.4 Unscheduled Visit.....	11
4.14 Efficacy Endpoints .....	11
4.14.1 Primary Efficacy Endpoint .....	11
4.14.2 Other Efficacy Endpoints.....	12
4.14.3 Definitions of Terms.....	14
4.14.3.1 Adverse Event.....	14
4.14.3.2 Suspected Adverse Reaction.....	14
4.14.3.3 Unexpected Adverse Event.....	14
4.14.3.4 Serious Adverse Event.....	14
4.14.3.5 Mandatory problem reporting.....	15
4.14.4 Assessment of Adverse Events .....	15
4.14.4.1 Assessment of Severity.....	15
4.14.4.2 Assessment of Causality .....	15
4.14.5 Reporting Safety Observations .....	15
<b>5 ETHICS .....</b>	<b>16</b>
5.1 Informed Consent .....	16
5.2 Institutional Review Board (IRB).....	16
5.3 Subject Confidentiality .....	16

<b>6</b>	<b>DATA HANDLING AND RECORDKEEPING.....</b>	<b>17</b>
6.1	Site Regulatory Documents Required for Initiation .....	17
6.2	Maintenance and Retention of Records .....	17
6.2.1	Case Report Forms (CRFs).....	17
6.2.2	Primary Source Documents .....	17
6.3	Study Monitoring.....	18
6.4	Completion of the Study.....	18
<b>7</b>	<b>CONFIDENTIALITY, USE OF INFORMATION, AND PUBLICATION .....</b>	<b>18</b>
<b>8</b>	<b>REFERENCES.....</b>	<b>19</b>
<b>9</b>	<b>APPENDIX 1.....</b>	<b>8</b>
<b>10</b>	<b>APPENDIX 2.....</b>	<b>9</b>

## **LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS**

<b><u>Term</u></b>	<b><u>Definition</u></b>
AE	Adverse event
CRF	Case report form, paper or electronic
EOS	End of study
GCP	Good Clinical Practice
ICF	Informed consent form
ICH	International Council for Harmonisation
IRB	Institutional Review Board
ITT	Intent-to-treat
OTC	Over-the-counter
PI	Principal investigator
PP	Per-protocol
SAE	Serious adverse event
TEAE	Treatment-emergent adverse event

## 2 INTRODUCTION

Diabetes Mellitus (DM) is a common and debilitating disease that also affects the skin.<sup>1,2</sup> Between 30% and 70% of patients with DM, both type 1 and type 2, will present with a cutaneous complication of DM. Dermatologic conditions linked with DM vary in severity and can be benign, deforming, and even life-threatening.<sup>1</sup> These skin conditions can offer insight into patients' glycemic control and may be the first sign of DM in undiagnosed patients. Recognition and management of these conditions is important in maximizing the quality of life and in avoiding serious adverse effects.

DM can be associated with pruritus, more often localized than generalized. Affected areas can include the scalp, ankles, feet, trunk, or genitalia. Pruritus is more likely in DM who have dry skin or diabetic neuropathy. Cutaneous disorders associated with DM commonly bother and cause pain and severely impact quality of life, including interpersonal relationships.<sup>1</sup>

CeraVe® Skincare contains a unique combination of three ceramides. Ceramides are key physiologic lipids required for construction and maintenance of the epidermal barrier.

## 3 STUDY OBJECTIVES

To evaluate the safety and efficacy of the *CeraVe*® Hydrating Cleanser and Moisturizing Cream for the improvement of dry skin in patients with diabetes mellitus.

## 4 INVESTIGATIONAL PLAN

### 4.1 Overall Study Design

This is a multicenter, open-label, cohort study designed to clinically evaluate the CeraVe® Hydrating Cleanser and Moisturizing Cream for the improvement of dry skin in patients with diabetes mellitus. All subjects meeting inclusion/exclusion criteria will receive unblinded product. This is a single cohort study, with no placebo or randomization schedule.

#### Visit Schedule:

Visit 1 / Day -30 to 0 – Screening\*

Visit 1 or 2 / Day 0 – Baseline\*

Visit 3 / Day 28 (± 5 days) – End of study (EOS)

\* Visits 1 and 2 may be combined to occur on same day.

#### Evaluations include:

1. Physician-assessed Dry Skin Classification Scale
2. Physician-assessed Global Aesthetic Improvement Scale
3. Subject-assessed Dry Skin Classification Scale
4. Subject satisfaction with treatment outcomes, regimen and product features
5. Safety will be assessed by monitoring adverse events (AEs) at all study visits

## 4.2 Number of Study Centers

Approximately 10 sites in the United States.

## 4.3 Duration of Participation

Subjects will participate in the study for approximately 28 ( $\pm$  5) days from the time they sign the informed consent form (ICF) through the EOS visit.

## 4.4 Duration of Study

The study will require approximately 6 months from the first subject signing the ICF to the EOS visit for the last subject.

## 4.5 Sample size

There is no formal sample size calculation for this study. The sample size is based on clinical considerations and not statistical power calculations. Sixty (60) subjects will be recruited.

## 4.6 Inclusion Criteria

1. Men or women between the ages of 18 and 75 years of age.
2. Willing to provide written informed consent.
3. A diagnosis of diabetes mellitus (DM).
4. DM-related dry skin changes such as xerosis or xeroderma.

## 4.7 Exclusion Criteria

1. History of allergy, anaphylaxis or hypersensitivity to any of the ingredients in CeraVe® Hydrating Cleanser or Moisturizing Cream.
2. History of allergic contact dermatitis secondary to cleansers or moisturizers.
3. Has a heightened immune response to common allergens, especially inhaled, topical or food allergens (atopy).
4. Has any clinical manifestation in the treatment area(s) or other disorders that, in the investigator's opinion, may affect assessments or results of the study products.
5. Inability to attend all study visits and follow treatment regimen.

## 4.8 Analysis Populations

- Intent-to-treat (ITT/safety) population: All enrolled subjects who received study products.
- Per-protocol (PP): All enrolled subjects who met all inclusion/exclusion criteria; received study products, completed all visits within the specified window; completed assessments and had no significant protocol violations that would affect the treatment evaluation.

Safety analyses will be performed on the ITT population. The frequency and percentage of subjects reporting adverse events (AEs) will be tabulated by preferred terms and further by severity and relationship to study product(s).

Efficacy analyses will be performed on the ITT and PP populations, with ITT as the primary population and PP supportive.

#### **4.9 Primary Endpoint**

The primary efficacy endpoints are the Physician-assessed Global Aesthetic Improvement Scale and Physician-assessed Dry Skin Classification Scale, at Visit 3.

#### **4.10 Beginning and End of Study**

A subject is considered to be enrolled in the study when he/she has provided written informed consent and has received the investigational products.

A subject is considered to have completed the study after he/she has completed Visit 3.

A subject is considered to have withdrawn after he/she has withdrawn consent or has been withdrawn under the conditions specified in Section 4.11.

A subject is considered to have been lost to follow-up if he/she cannot be contacted by the investigator. The investigator will document efforts to attempt to reach the subject. The end of participation for a subject lost to follow-up is documented as the date of last contact.

Each subject will be monitored for the occurrence of AEs, including serious adverse events (SAEs), starting immediately after the subject has received the investigational products. Each subject will be followed for safety monitoring until he/she is discharged from the study.

Follow-up procedures related to AEs or SAEs may continue beyond the end of the study.

Each subject will participate in the study for approximately 1 month. It is anticipated that the duration of this study will be 6 months from the first subject signing the ICF to the EOS visit last subject.

#### **4.11 Subject Withdrawal Criteria**

A subject may withdraw from the study at any time for any reason.

A subject will be withdrawn from the study if his/her safety or well-being is determined to be at risk. Withdrawal will be made at the discretion of the investigator or at the subject's request.

A subject must withdraw from the study for any of the following reasons:

- The subject withdraws consent
- There is a significant protocol violation as determined by the Sponsor or medical monitor.

A subject may be withdrawn from the study for any of the following reasons:

- Lost to follow-up
- Investigator discretion

Withdrawal is permanent; after a subject has been withdrawn, he/she will not be allowed to enroll again.



If a subject is withdrawn from the study for any reason, relevant information including the date and primary reason for withdrawal, must be documented on the EOS case report form (CRF) and source document.

If a subject withdraws from the study at any time due to an AE, the reason for withdrawal, the nature of the AE, and its clinical course must be fully documented. The investigator must strive to follow the subject until the AE has resolved, become clinically insignificant, is stabilized, or the subject is lost to follow-up. For any SAE, follow the procedures provided in Section 4.14.5.

#### **4.11.1 Replacement of Subjects**

A subject who withdraws from the study will not be replaced.

#### **4.12 Treatments**

The investigator will take responsibility for and will take all steps to maintain appropriate records and ensure appropriate supply, handling, storage, distribution, and use of study materials in accordance with the protocol and any applicable laws and regulations.

##### **4.12.1 Dosage and Formulations**

The study product will be used in the study and provided by the Sponsor:

A description of the investigational products are presented in Appendix 1 and 2.

##### **4.12.2 Method of Packaging, Labeling, Storage, and Dispensing**

The investigational products will be labelled as per the manufacturer's packaging. Products must be used prior to the expiration date printed on the package.

The investigator agrees to store and administer the study product only at the site approved by the independent research board (IRB). The investigator, sub-investigator(s), or qualified designees also agree that the study product will be administered only to subjects who have provided written informed consent and have met all entry criteria. Study product may not be used for any purpose other than as stated in the protocol.

##### **4.12.3 Study Products Accountability**

Study product will be available on site for each subject. Receipt of study product will be documented. The administration of study product will be recorded on the Study Product Dispensing Log. The site monitor will periodically check the supply of study product held by the investigator to ensure accountability.

Inventory records must be readily available for inspection by the study monitor and/or auditor, and open to inspection by regulatory authorities at any time.

##### **4.12.4 Prior and Concomitant Medications**

All medications, supplements, over-the-counter (OTC) products and other treatments taken by the subject during the study are to be recorded on the CRF using their generic name, if known, with the corresponding indication.

#### 4.12.5 Assessment of Compliance

Administration of the study product by the investigator is documented on the CRF.

Subject compliance with treatment regimen will be documented at Visit 3.

#### 4.13 Study Procedures

The schedule of study activities is summarized in Table 1.

All clinical assessments must be conducted by qualified investigators who have been delegated these tasks by the study Sponsor. The PI may delegate this task only to physicians who have documented training for this protocol and past experience conducting the assessment.

To minimize variability of evaluations, the same investigator/sub-investigator should perform these assessments for any given subject and anticipate evaluating the subject at each visit, to the extent possible.

A unique subject number will be assigned to each subject.

**Table 1. Study procedures.**

Visit	Visit 1	Visit 1 or 2	Visit 3
	Screening	Baseline	End of Study
Timeline	Day -30 to 0	Day 0	Day 28 +/- 5 days
Informed consent	X		
Concomitant medications and procedures	X		
Demographics	X		
Eligibility	X		
Physician-assessed Dry Skin Scale	X	X*	X
Daily product administration		X	X
Subject-assessed Dry Skin Scale		X	X
Subject-assessed quality of life measurements		X	X
Subject satisfaction questionnaires			X
Assessment of adverse events			X
Assessment of compliance			X

\*Skip this procedure if Visit 1 and 2 are combined on same day.

## Study Initiation

The investigational staff may not enroll any subjects prior to completion of a site initiation visit. This visit will include, but is not limited to, an inventory of study supplies (if present) and a detailed review of the protocol, CRFs, and the investigator's responsibilities.

### 4.13.1 Written Informed Consent

The study personnel will review the ICF with each subject and give the subject an opportunity to have all questions answered before proceeding with any study procedures. A copy of the signed ICF will be given to every subject and the original will be maintained with the subject's records.

### 4.13.2 Significant Medical History/Demographic Information

Medical history and demographic information will be obtained at Screening. The medical history will include a complete review of all current diseases and their respective durations and treatments. Demographic information will include date of birth, sex at birth and ethnicity.

### 4.13.3 Adverse Events and Serious Adverse Events Assessment

See Section 4.14.3.1 for instructions on the assessment and reporting of AEs and SAEs and Section 4.14.5. for instructions on reporting SAEs to the Sponsor.

### 4.13.4 Unscheduled Visit

An unscheduled visit is allowed at any time if in the investigator's opinion it is warranted. The following procedures may be performed at the Unscheduled Visit if required.

## 4.14 Efficacy Endpoints

### 4.14.1 Primary Efficacy Endpoint

The primary efficacy endpoint is the physician-assessed GAIS at Visit 3.

#### GAIS

GAIS Rating	Description	Score
Very much improved (3)	Optimal treatment result for the subject in this treatment area	
Much improved (2)	Marked improvement in appearance from the initial condition, but not completely optimal for this subject.	
Improved (1)	Obvious improvement in the appearance from the initial condition.	
No change (0)	The appearance in this treatment area is essentially the same as the original condition	
Worse (-1)	The appearance in this treatment area is worse than the original condition	
Much Worse (-2)	The appearance in this treatment area is markedly worse than the original condition	
Very Much Worse (-3)	The appearance in this treatment area is obviously worse than the original condition	

#### 4.14.2 Other Efficacy Endpoints

##### Physician-assessed Dry Skin Classification Scale

Signs & Symptoms	Score*
Skin is rough and/or scaling	
Skin is itching	
Skin is painful	
Erythema is present	
Fissures are present	

0-4 (0=none; 4=severe)

##### Subject-assessed Dry Skin Classification Scale

Signs & Symptoms	Score*
Skin is rough and/or scaling	
Skin is itching	
Skin is painful	
Erythema is present	
Fissures are present	

0-4 (0=none; 4=severe)

##### Subject satisfaction with treatment outcomes

*Overall level of satisfaction with product results (check one)*

Extremely satisfied	Satisfied	Neutral	Dis-satisfied	Extremely dissatisfied

### Subject satisfaction with treatment regimen

*Overall level of satisfaction with treatment regimen (check one)*

Extremely satisfied	Satisfied	Neutral	Dis-satisfied	Extremely dissatisfied

### Subject-assessed product features

*My skin feels sufficiently clean after using the cleanser*

Strongly disagree	Disagree	Neutral	Agree	Strongly agree

*My skin feels sufficiently moisturized after using the moisturizer*

Strongly disagree	Disagree	Neutral	Agree	Strongly agree

### Subject's overall assessment

*I would continue to use the treatment regimen outside of the study*

Strongly disagree	Disagree	Neutral	Agree	Strongly agree

### Quality of life assessments

Over the last week, how embarrassed or self conscious have you been because of your skin?

Very much	A lot	A little	Not at all

Over the last week, how much has your skin affected any social or leisure activities?

Very much	A lot	A little	Not at all

Over the last week, has your skin prevented you from working or studying?

Very much	A lot	A little	Not at all

#### **4.14.3 Definitions of Terms**

##### **4.14.3.1 Adverse Event**

An AE is defined as any untoward medical occurrence associated with the use of an investigational product in humans, whether or not considered product-related as per ICH E2D. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a product, without any judgment about causality.

##### **4.14.3.2 Suspected Adverse Reaction**

A suspected adverse reaction (SAR) is defined as any AE for which there is reasonable possibility that the product caused the AE (21 CFR 312.32 (a)).

##### **4.14.3.3 Unexpected Adverse Event**

An AE or SAR is considered unexpected if it is not consistent with the risk information described in the labeling for the study products.

##### **4.14.3.4 Serious Adverse Event**

An SAE is defined as any AE or SAR that, in the view of the investigator or Sponsor, results in any of the following outcomes (21 CFR 312.32 (a)):

- Death
- Life-threatening
- Inpatient hospitalization or prolongation of existing hospitalization.
- Persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
- Congenital anomaly/birth defect
- Required intervention to prevent permanent impairment/damage

#### 4.14.3.5 Mandatory problem reporting

All AEs must be documented in the CRFs and source documents. The qualified investigator is required to report serious adverse events to the study Sponsor within 72 hours of discovery.

#### 4.14.4 Assessment of Adverse Events

##### 4.14.4.1 Assessment of Severity

Severity of AEs will be graded according to the following definitions:

Mild: AE that was easily tolerated

Moderate: AE sufficiently discomforting to interfere with daily activity

Severe: AE that prevented normal daily activities

##### 4.14.4.2 Assessment of Causality

A medically qualified investigator must assess the relationship of any AE (including SAEs) to the use of the study product as unlikely related, possibly related, or probably related based on available information, using the following guidelines:

Unlikely related: no temporal association, or the cause of the event has been identified, or the study product cannot be implicated based on available information

Possibly related: temporal association but other etiologies are likely to be the cause; however, involvement of the study product cannot be excluded based on available information

Probably related: temporal association, other etiologies are possible, but unlikely based on available information.

#### 4.14.5 Reporting Safety Observations

Any S/AE must be reported to the Sponsor or designee by telephone, email or through the study portal (<https://medalogik.com>) as soon as possible after the investigator or coordinator has become aware of its occurrence. The investigator/coordinator must complete an S/AE Form.

Sponsor/Designee contact details:

Kaitlyn M. Enright Medical Monitor Cell: 514-248-7033 Email: <a href="mailto:Kaitlyn@rbccconsultants.com">Kaitlyn@rbccconsultants.com</a>
---

The investigator must be prepared to supply the medical monitor with the following information:

1. Investigator name and site number
2. Subject number
3. Subject initials and date of birth
4. Subject demographics

5. Clinical event
  - a. description
  - b. date of onset
  - c. severity
  - d. treatment (including hospitalization)
  - e. relationship to study product
  - f. action taken regarding study product
  - g. outcome, if known

## **5 ETHICS**

### **5.1 Informed Consent**

The principles of informed consent, according to TCPS 2 (2010) – 2<sup>nd</sup> edition of Tri-Council Policy Statement and the International Council on Harmonization (ICH) guidelines on GCP, will be followed. A copy of the proposed ICF must be submitted with the protocol to the IRB for approval.

The informed consent process must be conducted and the ICF must be signed before each subject undergoes any screening procedures that are performed solely for the purpose of determining eligibility for the study, in compliance with 21 CFR Part 50. Each subject's signed ICF must be kept on file by the investigator for inspection by regulatory authorities at any time. A copy of the signed ICF will be given to the subject. A notation will be made in the subject's medical record indicating the date informed consent was obtained.

### **5.2 Institutional Review Board (IRB)**

The study protocol and ICF must be approved in writing by an appropriate IRB as defined by the regulations and other applicable requirements prior to enrollment of any study subjects.

Any changes to the protocol or a change of investigator approved by the Sponsor must also be approved by the site's IRB and documentation of that approval provided to the Sponsor or designee. Records of the IRB review and approval of all documents pertaining to this study must be kept on file by the investigator and are subject to inspection by regulatory authorities during or after completion of the study. SAEs must also be reported to the IRB.

Periodic status reports must be submitted to the IRB at least annually, as well as notification of completion of the study and a final report within 1 month of study completion or termination. A copy of all reports submitted to the IRB must be sent to the Sponsor or designee.

The investigator will ensure that an IRB that complies with the requirements set forth in by the authorities and will be responsible for the initial and continuing review and approval of the study.

### **5.3 Subject Confidentiality**

All subject data will be identified only by a subject identification number and subject initials. However, in compliance with federal guidelines regarding the monitoring of clinical studies and in fulfillment of his/her obligations to the Sponsor, the investigator must permit the study



monitor, Sponsor representative or auditor, and/or FDA or other regulatory authority to review the portion of the subject's medical record that is directly related to the study. This shall include all study-relevant documentation including medical history to verify eligibility, admission/discharge summaries for hospital stays occurring while the subject is enrolled in the study, and autopsy reports if a death occurs during the study.

As part of the required content of informed consent, each subject must be informed that his or her medical chart may be reviewed by the Sponsor, the Sponsor's authorized representatives, FDA, or other regulatory authority. If access to the medical record requires a separate waiver or authorization, it is the investigator's responsibility to obtain such permission from the subject in writing before the subject is entered into the study.

## **6 DATA HANDLING AND RECORDKEEPING**

### **6.1 Site Regulatory Documents Required for Initiation**

The Sponsor or designee must receive the following documents prior to the initiation of the study:

- Current curricula vitae, signed and dated, for the principal investigator (PI) and any co-investigators
- Current license(s) number of the PI and co-investigators
- A copy of the protocol signature page signed by the PI

### **6.2 Maintenance and Retention of Records**

The study will be conducted according to GCP as outlined in ICH guidelines. It is the responsibility of the investigator to maintain a comprehensive and centralized filing system of all relevant documentation. Investigators will be instructed to retain all study records required by the Sponsor and the regulations in a secure and safe facility with limited access. Regulations require retention for a period of at least 7 years for studies investigating non-regulated products. These regulatory documents should be retained for a shorter/longer periods if required by local regulatory authorities.

These records include documents pertaining to the receipt and return of study product, IRB, informed consent, source documents, and final signed CRFs. No documents shall be destroyed without first notifying the Sponsor.

#### **6.2.1 Case Report Forms (CRFs)**

CRFs for individual subjects will be provided by the Sponsor or designee. CRFs must be legible and complete. CRFs for this study will be maintained in paper format and/or online in a fillable PDF document. All paper forms should be completed using a black ballpoint pen. Errors should be lined out, *but not obliterated*, and the correction inserted, initialed, and dated by designated study personnel.

#### **6.2.2 Primary Source Documents**

The investigator must maintain primary source documents supporting significant data for each subject's medical notes.

The investigator must also retain all subject-specific printouts/reports of procedures performed as a requirement of the study. During monitoring visits the monitor will validate CRF entries against these data sources.

### **6.3 Study Monitoring**

The Sponsor or designee will be responsible for virtually monitoring the study according to GCP and applicable regulations. The study will be monitored by a Clinical Research Associate (CRA) in compliance with GCP, ICH guidelines, and applicable regulations. The coordinator and/or investigator should be available to answer questions or resolve data clarifications.

### **6.4 Completion of the Study**

The investigator is required to forward CRFs and all other relevant data and records to the Sponsor or designee. The investigator will complete and report (submission of CRFs) his/her study in satisfactory compliance with the protocol as soon as possible.

The Sponsor will submit a final report to the IRB following study completion or early termination.

## **7 CONFIDENTIALITY, USE OF INFORMATION, AND PUBLICATION**

All information related to this study that is supplied by the Sponsor and not previously published is considered confidential information. This information includes but is not limited to data, materials (protocol, CRFs), equipment, experience (whether of a scientific, technical, engineering, operational, or commercial nature), designs, specifications, know-how, product uses, processes, formulae, costs, financial data, marketing plans and direct selling systems, customer lists, and technical and commercial information relating to customers or business projections used by the Sponsor in its business. Any data, inventions, or discoveries collected or developed as a result of this study are considered confidential. This confidential information shall remain the sole property of the Sponsor, shall not be disclosed to any unauthorized person or used in any unauthorized manner without written consent of the Sponsor, and shall not be used except in the performance of the study.

The information developed during the course of this study is also considered confidential and will be used by the Sponsor in the development of the study medication. The information may be disclosed as deemed necessary by the Sponsor. To allow the use of the information derived from this study, the investigator is obliged to provide the Sponsor with complete test results and all data developed in the study. The information obtained during this study may be made available to other investigators who are conducting similar studies.

The investigator shall not make any publication related to this study without the express written permission of the Sponsor. If the investigator wants to publish or present the results of this study, he or she agrees to provide the Sponsor with an abstract, manuscript, and/or presentation for review 60 days prior to submission for publication or presentation. The Sponsor retains the right to delete confidential information and to object to suggested publication/presentation and/or its timing (at the Sponsor's sole discretion).

## **8 REFERENCES**

1. Kirsner RS, Yosipovitch G, Hu S, Andriessen A. Diabetic skin changes can benefit from moisturizer and cleanser use: A review. *J Drugs Dermatol*. 2019;18(12):1211-1217.
2. Guenther L, Lynde CW, Andriessen A et al. Pathway to dry skin prevention and treatment. *J Cutan Med Surg* 2012;16(1):23-31

## 9 APPENDIX 1



### CeraVe Hydrating Cleanser Fact Sheet

Developed with dermatologists, CeraVe offers a complete line of skincare products that contain ceramides 1, 3 and 6-II to help restore the skin's natural protective barrier. **CeraVe Hydrating Cleanser** removes dirt and oil from the skin, leaving it cleansed and hydrated. Suitable for normal to dry skin.



**Hyaluronic Acid**  
Help retain skin's natural moisture

**MVE Delivery Technology**  
Controlled release for all day hydration

**Accepted by the National Eczema Association**

#### Key Features:

- Gentle cleanser that is non-drying.
- Formula is both fragrance-free and non-comedogenic.
- Hydrates skin and helps restore the skin's protective barrier.

#### How To Use:

- Wet skin with lukewarm water
- Massage cleanser into skin in a gentle, circular motion
- Rinse

#### 2021506 4 - Ingredients:

AQUA / WATER, GLYCERIN, CETEARYL ALCOHOL, PEG-40 STEARATE, STEARYL ALCOHOL, POTASSIUM PHOSPHATE, CERAMIDE NP, CERAMIDE AP, CERAMIDE EOP, CARBOMER, GLYCERYL STEARATE, BEHENTRIMONIUM METHOSULFATE, SODIUM LAUROYL LACTYLATE, SODIUM HYALURONATE, CHOLESTEROL, PHENOXYETHANOL, DISODIUM EDTA, DIPOTASSIUM PHOSPHATE, TOCOPHEROL, PHYTOSPHINGOSINE, XANTHAN GUM, CETYL ALCOHOL, POLYSORBATE 20, ETHYLHEXYLGLYCERIN (Code F.I.L D214629/4)

#### DID YOU KNOW?

The skin naturally contains ceramides that may become depleted over time, contributing to dry and irritated skin.

#### WHAT ARE CERAMIDES?

Part of the glue that holds skin cells together, ceramides keep moisture in and irritants out, while maintaining the skin's barrier. To replenish the vital ceramides healthy skin needs, CeraVe products are formulated with ceramides 1, 3 & 6-II

#### HOW DOES IT WORK?

CeraVe products use patented Multivesicular Emulsion (MVE) technology that releases ingredients slowly over time, allowing them to absorb into the skin to hydrate & nourish as well as restore & maintain the skin's natural barrier.

10 APPENDIX 2



## CeraVe Moisturising Cream Fact Sheet

Developed with dermatologists, CeraVe offers a complete line of skincare products that contain ceramides 1, 3 and 6-II to help restore the skin's natural protective barrier. **CeraVe Moisturising Cream** is a rich, non-greasy formula that provides all-day hydration with a soft, powdery finish and helps restore the protective skin barrier. Suitable for dry to very dry skin on the face and body.



**Hyaluronic Acid**  
Helps retain skin's natural moisture



**MVE Delivery Technology**  
Controlled release for all day hydration



**Accepted by the National Eczema Association**

### Key Features:

- Formulated with Hyaluronic Acid to help retain skin's natural moisture.
- Features an oil-free formula with hyaluronic acid that is non-comedogenic.

**How To Use:** Apply liberally as often as needed.

### 2021500 - Ingredients:

AQUA / WATER, GLYCERIN, CETEARYL ALCOHOL, CAPRYLIC/CAPRIC TRIGLYCERIDE, CETYL ALCOHOL, CETEARETH-20, PETROLATUM, POTASSIUM PHOSPHATE, CERAMIDE NP, CERAMIDE AP, CERAMIDE EOP, CARBOMER, DIMETHICONE, BEHENTRIMONIUM METHOSULFATE, SODIUM LAUROYL LACTYLATE, SODIUM HYALURONATE, CHOLESTEROL, PHENOXYETHANOL, DISODIUM EDTA, DIPOTASSIUM PHOSPHATE, TOCOPHEROL, PHYTOSPHINGOSINE, XANTHAN GUM, ETHYLHEXYLGLYCERIN (Code F.I.L. D213768/2)

### DID YOU KNOW?

The skin naturally contains ceramides that become depleted over time, leading to dry and irritated skin.

### WHAT ARE CERAMIDES?

Part of the glue that holds skin cells together, ceramides help skin keep moisture in and irritants out, while maintaining the skin's barrier. To replenish the vital ceramides healthy skin needs, CeraVe products are formulated with ceramides 1, 3 & 6-II.

### HOW DOES IT WORK?

CeraVe products use patented Multivesicular Emulsion (MVE) technology that releases ingredients slowly over time, allowing them to absorb into the skin to hydrate & nourish, as well as restore & maintain the skin's natural barrier.