Title	An open-label study to assess efficacy and safety of a Healing Ointment when used on infants with mild-to-moderate diaper rash
Protocol number	GLI.04.US.SL.027
Sponsor name and address	Galderma Laboratories, L.P. 2001 Ross Avenue, Suite 1600 Dallas, TX 75201 USA
Study product	Cetaphil® Healing Ointment Fla#1748 (ref.:B50H48)
Investigator agreement	I have read the clinical study described herein, recognize its confidentiality, and agree to conduct the described study in compliance with Good Clinical Practices (GCP), the ethical principles contained within the Declaration of Helsinki, this protocol, and all applicable regulatory requirements.
Principle Investigator	
	Signature Date
Investigator name	Latanya Benjamin, MD, FAAD, FAAP
Address	Young Skin 5451 N University Drive, Suite #103 Coral Springs, FL 33067 Phone: (954) 242-4275

AN OPEN-LABEL STUDY TO ASSESS EFFICACY AND SAFETY OF A HEALING OINTMENT WHEN USED ON INFANTS WITH MILD-TO-MODERATE DIAPER RASH

APPROVAL SIGNATURE PAGE

Latanya Benjamin, MD, FAAD, FAAP Principle Investigator Young Skin	Date
Sindhu Garimella, MS, CCRC Advisor Galderma Laboratories, L.P.	Date
Thu Q. Nguyen, PhD Medical Manager Galderma Laboratories, L.P.	Date
Christine Emesiani, PharmD Medical Affair Advisor Galderma Laboratories, L.P.	Date
Matthew Meckfessel, PhD Director, Medical Affairs Galderma Laboratories, L.P.	Date

1. SYNOPSIS

Clinical Study Title:	An open-label study to assess efficacy and safety of a Healing Ointment when used on infants with mild-to-moderate diaper rash
Clinical Trial Number:	GLI.04.US.SL.027
Indication:	Dermatitis
Study population:	Infants at 2-~~24~~ 35 months of age
Country(ies) Involved and Planned Number of Study Centers:	USA Site: Young Skin 5451 N University Drive, Suite #103, Coral Springs, FL 33067
Number of Subjects:	30 subjects to complete
Clinical Study Design:	This is a single-center, open-label study. Subjects and their parent/legal guardians will report to the site at baseline (day 0) visit, will be given an informed consent form, HIPAA form, photography release form, and medical history form to complete. Subjects will be screened on the basis of the selection criteria for study qualification. Efficacy assessment (skin health, skin smoothness, skin texture), tolerability assessment (dryness, peeling, edema), and self-assessment questionnaire will be performed. Subjects' parent/legal guardians will be instructed to apply the provided Healing Ointment to the buttocks and groin area (if applicable) at every diaper change. Subjects and their parent/legal guardians to return to the site at day 7 (± 3 days) and day 21 (± 3 days) for follow-ups. For each follow-up visit, investigator will perform objective assessments, tolerability assessments, and photography, if consented. Subjects' parent/legal guardians will perform self-assessment questionnaire. A subject and their parent/legal guardian will be involved in the study for 3 weeks.
Primary Effectiveness Objective and Endpoint:	To evaluate efficacy of a Healing Ointment in skin texture and smoothness in infants 2 to ~~24~~ 35 months old with mild to moderate diaper dermatitis

Secondary Effectiveness Objective(s) and Endpoint(s):	To evaluate subject satisfaction using a Self-Assessment Questionnaire.
Safety Objective and Endpoint	To evaluate safety and adverse events (AEs) throughout the study.
Clinical Study Duration:	The planned clinical study duration (from FSFV to LSLV) is approximately 9 weeks. The planned duration of recruitment is approximately 6 weeks.
Duration of Subject Participation:	Clinical study participation for each subject is 3 weeks
Inclusion criteria:	The subjects must meet all the following criteria to be eligible for the study: 1. Infant subjects aged 2 months to ~~24~~ 35 months 2. Females and males 3. All Fitzpatrick skin types I-VI 4. All races and ethnicities 5. Subject diagnosed with mild-to-moderate diaper rash 6. Subject with healthy immune systems 7. Willing to be photographed at each visit (optional) 8. Willing to abstain from use of any other topical diaper rash treatments (ointments, moisturizers, emollients, creams, and wipes) other than the assigned test product and skincare products that have been routinely used on the diaper area during the duration of the study 9. Willing to continue using regular brands of face/body cleanser and not to begin use of any new skincare products other than the test product for the duration of the study 10. Parent/legal guardian/legal guardians must be at least 18 years old and are willing and able to present proof of legal guardianship 11. Parent/legal guardian/legal guardian with ability to read, understand and give consent for participation in the study 12. Parent/legal guardians/legal guardians willing to sign a photography release form 13. Parent/legal guardian/guardian must agree to adhere to the procedures and requirements of the study and to report to the site on the day(s) and at the time(s) scheduled for the assessments
Exclusion criteria:	The presence of any of the following exclusion criteria excluded a subject from enrollment in the study: 1. Subject diagnosed with severe diaper rash

	2. History of allergy or hypersensitivity to any ingredient of the test product 3. Presence of any disease or lesions near or on the area to be treated, e.g., a. Inflammation, active, or chronic infection in or near the treatment area b. Psoriasis, eczema, rosacea, atopic dermatitis, herpes zoster/herpes simplex, and acanthosis c. Scars or deformities 4. History of coexisting bacterial infections or medical conditions with uncontrolled gastrointestinal diseases and/or bowel movements 5. History of severe elastosis and/or excessive sun exposure that, in the opinion of the Investigator, could have affected the outcome of the study 6. Planning on having surgeries and/or invasive medical procedures during the course of the study 7. Treatment with chemotherapy, immunosuppressive agents, inhaled corticosteroids, immunomodulatory therapy (e.g., monoclonal antibodies or antiviral treatment for human immunodeficiency virus or hepatitis C) 8. Current use of topical corticosteroids, topical prescription, or oral antibiotics in the treatment area, or use within last 2 weeks 9. Current use of over-the counter topical medications for diaper rash 10. History of cancer or previous radiation near or on the treatment area 11. Human immunodeficiency virus positive or active hepatitis 12. Presence of dermal markings on or near the treatment area that, in the opinion of the Investigator, will interfere with the clinical assessments 13. Any medical condition that, in the opinion of the Investigator, would make the subject unsuitable for inclusion (e.g., a chronic or relapsing, disease that may interfere with the outcome of the study) 14. Other condition preventing the subject from entering the study in the Investigator's opinion, (e.g., subjects failing baseline assessments, subjects not likely to avoid other cosmetic treatments in the treatment area, subjects anticipated to be unavailable or incapable of understanding the study assessments or having unrealistic expectations of the treatment result). 15. Study site personnel, close relatives of the study site personnel (e.g., parent/legal guardians, children, siblings, or spouse), or employees and close relatives of employees at the Sponsor company. 16. Participation in any interventional clinical study within 30 days of screening
Investigational Products:	Cetaphil Healing Ointment Fla#1748 (ref.:B50H48)
Treatment Area / Treatment Regimen / Mode of Administration	Healing Ointment will be applied topically to the rash area with every diaper change

Effectiveness Assessments:	Clinical Grading • Efficacy assessment of skin health, skin smoothness, skin texture compared to baseline Self-Assessment Questionnaire • Parent/legal guardian assessment
Safety Assessments:	Tolerability assessment of dryness, peeling, edema Safety/tolerability assessment at each visit Adverse Event reporting: AEs will be obtained from signs and symptoms reported by the subject or detected during each examination.
Statistical Methods:	In general effectiveness, safety and baseline characteristics variables will be presented using descriptive statistics within each treatment group and in combination, and graphs as appropriate. Continuous endpoints will be summarized using descriptive statistics, e.g., mean, median, standard deviation, minimum and maximum values. Categorical endpoints will be presented in frequency tables with number and percentage of observations for each level.

2. TABLE OF CONTENTS

2. LIST OF ABBREVIATIONS AMD DEFINITION OF TERMS

AE	Adverse Event
CTA	Clinical trial agreement
CTN	Clinical trial number
CV	Curriculum vitae
EC	Ethics Committees
EOS	End of Study
FSFV	First Subject First Visit, i.e. first subject who signs the informed consent form
FST	Fitzpatrick Skin Type
GCP	Good Clinical Practice
GDPR	General Data Protection Regulation
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IFU	Instructions for use
Investigational product	Medical device being assessed for safety or performance in a study. “Investigational product” is the same as “study device”, “investigational device”, or “investigational medical device.”
Investigator	The Principal Investigator (PI) or other qualified person, i.e. sub-Investigator, designated and supervised by the PI at a study site to perform critical study-related procedures or to make important study-related decisions as specified on the signature and delegation log
Investigator file	Essential documents relating to a clinical study as defined in applicable GCP guidance document and maintained by the Investigator.
ISO	International Organization for Standardization
ITT	Intention-to-treat
LSFV	Last Subject First Visit
LSLV	Last Subject Last Visit
PI	Principal Investigator; qualified person responsible for conducting the study at a study site
SAE	Serious Adverse Event
Study products	The products used for treatment in the study
Study site	Institution or site where the study is carried out
Tx	Treatment
WHO	World Health Organization

3. BACKGROUND AND RATIONALE

Diaper dermatitis is the most common skin disorder seen in young infants and affects those using diapers.[1] Increased moisture resulting from wearing diapers leads to increased friction and maceration, making the skin more susceptible to damage.[2] Infants with diaper dermatitis can present with erythema, edema, scaling, peeling, papules and dryness, and diagnosis is based on skin findings.[1] Management of diaper dermatitis must both heal damaged skin and prevent rash recurrence. The use of topical emollients is recommended to improve skin barrier function, prevent over-hydration, and provide a barrier between the skin and the diaper, limiting contact with the skin. It is recommended to apply emollients with every diaper change.[1]

Cetaphil® Healing Ointment (Galderma, Dallas, TX) is an Over-the-Counter (OTC) skin protectant that contains 71.5% petrolatum, shea butter to soften, smooth and hydrate, as well as vitamin E to help support moisture barrier function. The Healing Ointment has been clinically proven to hydrate the skin's natural barrier for 48 hours while quickly protecting and healing dry, cracked, irritated skin for visible improvement in 1 week. The product is also hypoallergenic, non-comedogenic, gentle on sensitive skin and accepted by the National Eczema Association. These beneficial properties make Cetaphil® Healing Ointment an ideal candidate as a treatment for diaper rash in infants. This study is to investigate safety and efficacy of Cetaphil® Healing Ointment on infants with diaper rash.

4. STUDY OBJECTIVES AND CLINICAL HYPOTHESIS

4.1 Study Objectives

The primary objective of this study is:

- To evaluate benefits of a Healing Ointment in skin improvement in infants 2 to ~~24~~ 35 months old

The secondary objectives of this study are:

- To evaluate subject satisfaction using a self-assessment questionnaire
- To evaluate safety throughout the study

4.2 Clinical Hypothesis

The Sponsor's test material will produce a statistically significant improvement in clinical grading of efficacy parameter scores over the course of 3 weeks of use when compared with baseline scores/values. Additionally, the Sponsor's test material will be well tolerated by the subjects, with no statistically significant increases in scores for tolerability/safety parameters at any study time point when compared with baseline scores. Furthermore, the Sponsor's test material will be well perceived by the subjects' parent/legal guardians according to a self-assessment questionnaire at day 1, week 1 and week 3, with a statistically significant proportion of favorable responses compared to unfavorable responses.

5. OVERALL STUDY DESIGN

This is a single-center, open-label study to evaluate the efficacy and tolerability of a Healing Ointment when used on infants with mild-to-moderate diaper rash.

Subjects and their parent/legal guardians will report to the site at baseline (day 0) visit, will be given an informed consent form, HIPAA form, photography release form, and medical history form to complete.

Subjects will be screened on the basis of the selection criteria for study qualification. Efficacy assessment (skin health, skin smoothness, skin texture), and tolerability assessment (erythema, dryness, scaling, peeling, edema) will be performed, and baseline photographs will be taken.

Subjects' parent/legal guardians will be instructed to apply the provided Healing Ointment to the groin and buttocks area at every diaper change.

Subjects' parent/legal guardians will complete Day 1 questionnaire at home. Subjects and their parent/legal guardians to return to the site at day 7 (± 3 days) and day 21 (± 3 days) for follow-ups.

For each follow-up visit, Investigator will perform assessments and photography. Subjects' parent/legal guardians will perform self-assessment questionnaire.

A subject and their parent/legal guardian will be involved in the study for 3 weeks. The study visits are illustrated in **Error! Reference source not found.**.

Figure 1. Study Flow Chart

6. SELECTION AND DISPOSITION OF STUDY POPULATION

6.1 Number of Subjects

An appropriate number of subjects meeting inclusion/exclusion criteria listed below will be enrolled on the study to achieve maximum 30 subjects who complete the study as planned.

6.2 Study Population Characteristics

- Healthy infant males and females with diaper rash

6.3 Inclusion Criteria

1. Subjects of 2-~~24~~ 35 months of age
2. Females and/or males
3. Subjects of any race and ethnicities
4. Subjects diagnosed with mild-to-moderate diaper rash
5. Subjects of any Fitzpatrick skin types I-VI
6. Subjects with healthy immune systems
7. Willing to be photographed at each visit (optional)
8. Willing to abstain from use of any other topical diaper rash treatments (ointments, moisturizers, emollients, creams, and wipes) other than the assigned test product and skincare products that have been routinely used on the diaper area during the duration of the study
9. Willing to continue using regular brands of face/body cleanser and not to begin use of any new skincare products other than the test product for the duration of the study
10. Parent/legal guardian/legal guardians must be at least 18 years old and are willing and able to present proof of legal guardianship
11. Parent/legal guardian/legal guardian with ability to read, understand and give consent for participation in the study
12. Parent/legal guardians/legal guardians willing to sign a photography release form
13. Parent/legal guardian/guardian must agree to adhere to the procedures and requirements of the study and to report to the site on the day(s) and at the time(s) scheduled for the assessments

6.4 Exclusion Criteria

1. Subject diagnosed with severe diaper rash
2. History of allergy or hypersensitivity to any ingredient of the test product
3. Presence of any disease or lesions near or on the area to be treated, e.g.,
    a. Inflammation, active, or chronic infection in or near the treatment area
    b. Psoriasis, eczema, rosacea, atopic dermatitis, herpes zoster/herpes simplex, and acanthosis
    c. Scars or deformities

4. History of coexisting bacterial infections or medical conditions with uncontrolled gastrointestinal diseases and/or bowel movements
5. History of severe elastosis and/or excessive sun exposure that, in the opinion of the Investigator, could have affected the outcome of the study
6. Planning on having surgeries and/or invasive medical procedures during the course of the study
7. Treatment with chemotherapy, immunosuppressive agents, inhaled corticosteroids, immunomodulatory therapy (e.g., monoclonal antibodies or antiviral treatment for human immunodeficiency virus or hepatitis C)
8. Current use of topical corticosteroids, topical prescription, or oral antibiotics in the treatment area, or use within last 2 weeks
9. Current use of over-the counter topical medications for diaper rash
10. History of cancer or previous radiation near or on the treatment area
11. Human immunodeficiency virus positive or active hepatitis
12. Presence of dermal markings on or near the treatment area that, in the opinion of the Investigator, will interfere with the clinical assessments
13. Any medical condition that, in the opinion of the Investigator, would make the subject unsuitable for inclusion (e.g., a chronic or relapsing disease that may interfere with the outcome of the study)
14. Other condition preventing the subject from entering the study in the Investigator's opinion, (e.g., subjects failing baseline assessments, subjects not likely to avoid other cosmetic treatments in the treatment area, subjects anticipated to be unavailable or incapable of understanding the study assessments or having unrealistic expectations of the treatment result).
15. Study site personnel, close relatives of the study site personnel (e.g., parent/legal guardians, children, siblings, or spouse), or employees and close relatives of employees at the Sponsor company.
16. Participation in any interventional clinical study within 30 days of screening

6.5 Concomitant Therapies

All treatments and therapies used 30 days prior to enrollment (Visit 1) or 90 days prior to enrollment for biologics and all treatments or therapies used during the course of the study must be recorded in the Case Report Form (CRF) or electronic Case Report Form (eCRF).

6.5.1. Authorized Therapies

Unless listed under the exclusion criteria (see Section 6.4) or in Prohibited Therapies (see Section 6.5.2), other therapies to treat ongoing conditions are authorized.

6.5.2. Prohibited Therapies

None other than as specified in the Inclusion/Exclusion criteria.

The decision to administer a prohibited medication/treatment should be made with the safety of the subject being the primary consideration. Whenever possible, Galderma Laboratories, L.P.

should be notified before the prohibited medication/treatment is administered to discuss possible alternatives.

If a subject receives prohibited therapy during the study, the subject may be allowed (at the discretion of the Investigator / Galderma Laboratories, L.P.) to continue in the study for safety evaluation purposes, only.

7. STUDY TREATMENT

The term "study treatment" refers to the study products (see Section 7.1)

7.1 Study Product Identification and Use

Study product: Cetaphil® Healing Ointment	
Form	Opaque ointment
Mode of administration	Topical application
Formula code	1748
Formula number	B50H48
Lot numbers	To be added upon study completion
Storage and handling	Store at room temperature 15-30°C (or 59-86°F), away from sunlight

7.2 Study Product Accountability

Upon receipt of the study products, the Investigator or designee will conduct an inventory. In accordance with federal regulations, the Investigator must agree to keep all test article in a secure location with restricted access. Designated study personnel will provide the test article to the subjects in accordance with the protocol.

During the study, the Investigator must maintain records of study treatment dispensation and collection for each subject. This record must be made available to the study monitor for the purposes of verifying the accounting of clinical supplies. Any discrepancies and/or deficiencies between the observed disposition and the written account must be recorded along with an explanation. At the conclusion of the study, the Investigator will be responsible for returning all unused study products (i.e., Cetaphil® product) unless otherwise instructed by the Sponsor. Shipping label and cost will be provided to the Investigator by the Sponsor.

7.3 Method of Treatment and Product Assignment

Subjects will be numbered sequentially in the order in which they qualify for entry into the study.

7.4 Treatment Product Dispensing

All treatment products will be administered only to subjects enrolled in the study, at no cost to subjects, and in accordance with the conditions specified in the protocol.

7.5 Treatments Compliance

Subjects will complete a daily diary, recording treatment product applications and comment during the study. Treatment product and diaries will be dispensed to subjects at Day 0 and reviewed for compliance at Day 7 and Day 21 visits. Treatment product will be visually inspected and weighed prior to distribution at Day 0. Subjects will be instructed to return the treatment product and daily diary at Day 7 and Day 21 visits. If subjects do not return their treatment product or diary at the study visits, a verbal confirmation will be obtained for usage compliance, and it will be documented as a note to file. Any suspected noncompliance with the treatment product or study instructions will be addressed by the Investigator or clinic staff. The Investigator will determine whether a subject's noncompliance will affect the study outcome and whether the data should be excluded from statistical analyses.

8. TREATMENT OF SUBJECTS

8.1 Informed Consent Form

An IRB-approved informed consent form (ICF) will be given to each prospective subject before participation in any study procedures. Prospective subjects will be given as much time as needed to read the ICF and will have the opportunity to have any study-related questions answered to their satisfaction prior to signing the ICF. If further questions exist, prospective subjects will be given sufficient time during the visit to have questions regarding the study and/or the ICF answered by the Investigator or study coordinator prior to signing.

8.2 Subject Identification

Enrolled subjects will be assigned a number that will uniquely identity every subject on the study. The numbers will remain with the subject throughout the study and should be used in all references to the individual in this study.

8.3 Subject Instructions for the Study

Subjects will be provided with the following instructions to follow during the study:

8.3.1. Study Product Usage Instructions

- Apply the provided treatment product liberally to rash area of your child with every diaper change. Reapply as needed throughout the day.
- Subject's parent/legal guardian will complete a daily diary, recording time, number of diaper changes, and number of applications to ensure treatment compliance.

8.3.2. Subject Instructions for Study Visits

- Subjects must show up to the study site with clean test area.
- Subject's parent/legal guardian must stop using any topical diaper rash treatment products and replace them with the provided study product.
- Bring the test product and daily diary with you to every visit.

8.3.3. General Study Instructions

- Throughout the study, parents/legal guardians must ensure subjects to avoid extended periods of sun exposure. Extra care should be taken to wear sunscreen and accessories (i.e., hat) and avoid sun exposure from 10 am to 3 pm.
- Do not use any topical diaper rash and/or moisturizing products on the test area (such as sunscreen, lotion, cream, oil, ointment, wipes), other than the assigned study product, for the duration of the study.
- Do not start using any new body care products other than the provided study product.
- Parents/legal guardians must use the same type of diapers for the duration of the study.

9. STUDY PROCEDURES

There will be 3 visits during the course of the study:

1. Visit 1 – Baseline/Day 0
2. Visit 2 – Week 1/Day 7 (follow-up)
3. Visit 3 – Week 3/Day 21 (end of study or EOS)

Table 1. Study Visits and Assessments

Procedure	Visit 1	Visit 2	Visit 3
	Day 0	Week 1 or Day 7	Week 3 or Day 21
	Screening/Baseline	**Follow-up**	**Follow-up**
Informed consent	X		
Demographic	X		
Inclusion and exclusion criteria	X		
Concomitant medications	X	X	X
Digital photography	X	X	X
Safety assessment	X	X	X
Efficacy assessment	X	X	X
Self-assessment questionnaire	X*	X	X
Adverse events		X	X
Study product	W/D	I/W/D	I/C/W
Subject diary	D	C/R/D	C/R

**At home questionnaire after first application.*
For products and daily diaries: D=Distribute, C=Collect, R=Review, W=Weigh, and I=Inspect (visually)

9.1 Visits

9.1.1. Visit 1 (Screening/Baseline / Day 0)

The following screening assessments will be performed:

- Obtain ICF, HIPAA form, and photography release form prior to conducting any study specific activity.

Note: Prior to beginning of any study related activities, subjects will be informed about the purpose and nature of the study, the expected post-treatment events, and the potential risks involved with the treatments. Once subjects have completed reading, they will be interviewed to ensure their understanding of the aforementioned forms and be given the opportunity to ask any study related questions. Subjects declining to sign any of the forms will be dismissed from the study.

- Assess eligibility: review inclusion/exclusion criteria. Subjects failing to meet criteria will be dismissed from the study.
- Record the subject's demographic information, medical history, and concomitant medications.

Once the subject is deemed eligible by the Investigator, the following procedures should be completed:

- Perform Clinical Grading and tolerability assessment as described in Section **Error! Reference source not found.** and 11.3.
- Digital photography will be completed as described in Section 10.2, if subject's parent/legal guardian consents.
- Dispense study product and diary. Instruct subject's parent/legal guardian on product application and diary completion. Remind subject's parent/legal guardian to complete the Day 1 questionnaire at home, and to bring the study products and diary to the next on-site visit.
- Schedule the next Visit 2 (Week 1).

9.1.2. Visit 2 (Week 1 ± 1 days)

- Confirm the subject's concomitant medications.
- Collect, weigh, and redistribute the study products.
- Collect, review, and distribute the diary.
- Interview subjects regarding any AEs that have occurred since starting study product application.
- Perform Clinical Grading and tolerability assessment as described in Section **Error! Reference source not found.** and 11.3.
- Digital photography will be completed as described in Section 10.2, if subject's parent/legal guardian consents.
- Instruct the subject to complete self-assessment questionnaire as described in Section 10.3.

- Schedule the next follow-up Visit 3 (Week 3 ± 3 days).

9.1.3. Visit 3 (Week 3 ± 3 days)

- Review the subject's concomitant medications.
- Collect, weigh, and retain the study products.
- Collect and review the diaries.
- Interview subjects regarding any AEs that have occurred since starting study product application.
- Perform Clinical Grading and tolerability assessment as described in Section **Error! Reference source not found.** and 11.3.
- Digital photography will be completed as described in Section 10.2, if subject's parent/legal guardian consents.
- Instruct the subject to complete self-assessment questionnaire as described in Section 10.3.
- Once completed, subjects will be dismissed from the Clinic.

9.2 Discontinued Subjects

Any subject is free to discontinue his/her participation in this study at any time and for whatever reason, specified or unspecified, and without prejudice.

An Investigator may decide to discontinue a subject from the study for safety reasons or when it is in the best interest of the subject. Galderma Laboratories, L.P. may also decide to prematurely terminate or suspend the study or the participation of a subject in the study. All data gathered on the subject prior to termination should be made available to Galderma Laboratories, L.P.

Criteria for the discontinuation of a subject during the study will include the following:

- Adverse Event
- Lack of Effect
- Pregnancy
- Subject Request
- Protocol Violation
- Lost to Follow-up
- Any unmanageable factor, in the Investigator's opinion, that may significantly interfere with the protocol or interpretation of results.

The reason and date for withdrawal should be documented in the subject's source documents and CRFs. When possible, an explanatory comment should be added to further explain the reason for the withdrawal. If withdrawal of a subject occurs during a regular study visit, the CRF for that specific visit shall be completed as far as possible.

If a subject is withdrawn from the study, all data collected until the time of withdrawal will be used in the analyses. Subjects who receive study products and are withdrawn or discontinued from the study will not be replaced. For AEs still ongoing at the time of withdrawal, see Section 13.

10. EFFECTIVENESS ASSESSMENTS

The methods for collecting effectiveness data are described in this section. To minimize inter-observer variability, every effort should be made to ensure that preferably the same individual who makes the initial baseline assessments completes all corresponding follow-up evaluations.

The methods for collecting effectiveness data are:

- Efficacy Grading
- Self-Assessment Questionnaire
- Tolerability Grading

10.1 Clinical Grading by Investigator

Investigator will grade tactile smoothness and skin texture parameters using a 10-point Griffiths' scale[3] where 0 = Excellent (best possible condition), 1-3 = Good, 4-6 = Fair, 7-9 = Poor (worst possible condition), as described in Table 2.

Table 2. Grading Scale for Tactile Smoothness and Skin Texture

Parameters	Excellent	Good			Fair			Poor		
	0	1	2	3	4	5	6	7	8	9
Skin Smoothness (tactile)	No palpable skin roughness, drag, and/or surface bumps, depressions	Mild palpable skin roughness, drag, and/or surface bumps, depressions			Moderate palpable skin roughness, drag, and/or surface bumps, depressions			Significantly (severe) palpable skin roughness, drag, and/or surface bumps, depressions		
Skin texture	Smooth visual skin texture	Slightly coarse and uneven skin texture			Moderately coarse and uneven skin texture			Severely coarse and uneven skin texture		

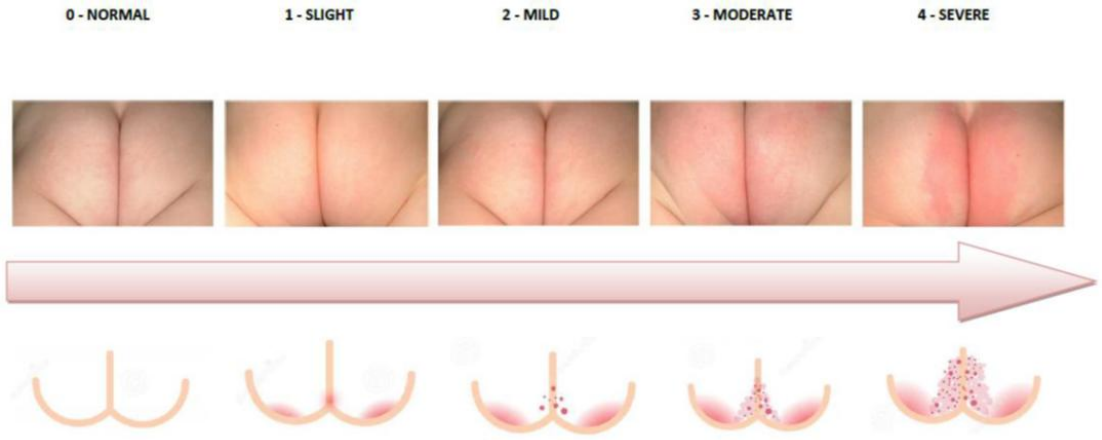
Investigator will grade diaper dermatitis parameter using a 5-point scale where 0 = Normal (no sign) and 4 = Severe (worst possible condition), as described in Table 3~~Table 3~~.

Table 3. Grading Scale for Diaper Dermatitis

Parameters	Normal	Slight	Mild	Moderate	Severe
	0	1	2	3	4
Diaper dermatitis	No clinical sign	Faint to definite pinkness over small area, may be a single raised bump (papule), may be slight dryness	Faint to definite pinkness over small area, definite redness over a very small area, scattered raised bumps (papule),	Faint to definite pinkness in a larger area, definite redness over a small area, very intense redness in a very small	Definite redness in a larger area, very intense redness in a very small area, single to several areas of raised bumps (papules), presence of

			moderate dryness	area, scattered raised bumps (papules), moderate dryness	erosions, may have slight peeling, may have swelling (edema), may have scaling

Figure 2. Visualization Corresponding to the Grading Scale for Diaper Dermatitis



10.2 Digital Photography

With subject's parent/legal guardian's consent, photographs will be taken prior to treatments with study product and at every follow-up visit in order to document treatment effect. Site personnel will be thoroughly trained in the photographic equipment and techniques before study start. All photographs will be taken zoomed into the area to the extent that no body part is distinguishable.

Camera equipment will be provided by the Sponsor or their designee and standardized photographs should be achieved. Further details regarding photography procedure will be specified in a separate user guide.

10.3 Self-Assessment Questionnaire

Subjects' parent/legal guardians will be asked about their perception and satisfaction with the study product using a self-assessment questionnaire after the first application and at each visit (see Appendix II).

11. SAFETY ASSESSMENTS

Safety assessments for this study include an evaluation and an interview of the subjects' parent/legal guardians at each visit to obtain information about any medical occurrence that meets the definition of an AE, and a subject diary. In addition, Investigator will perform tolerability assessment to grade the degree of irritation.

11.1 Assessment of AEs by Direct Questioning to Subject

Each subject's parent/legal guardian should be questioned about AEs at each visit following treatment. Definition and reporting requirements are found in Section 13.

11.2 Subject Diary

A subject diary will be dispensed to all subjects' parent/legal guardians for daily completion. The subject's parent/legal guardian will be specifically instructed to record presence of any symptoms that occur in the product application areas. Diary data will be counted and displayed separately from other AE data.

11.3 Tolerability Assessment

Tolerability assessments will be performed by Investigator at each visit prior to treatments with study product and at every follow-up visit. Investigator will grade the degree of irritation parameters that they observe in subject based on a 4-point analog scale, described in Table 4~~Table 4~~ (with half-point scores used as necessary to better describe the clinical condition).

Table 4. Tolerability Assessment Scale

Parameters	Score 0	Score 1	Score 2	Score 3
Dryness	None	Mild	Moderate	Severe
Peeling	None	Mild	Moderate	Severe
Edema	None	Mild	Moderate	Severe

12. STATISTICAL ANALYSIS

12.1 General

All study data will be listed in subject data listings.

All statistical analyses, including summary tables and data listings, will be performed. Confidence intervals will be two-sided and constructed at a confidence level of 95%. Statistical tests will be performed at a significance level of 5%, and *p* values will be two-sided.

All endpoints will be summarized descriptively including N, mean, median, standard deviation, minimum and maximum values, for the observed value as well as the change from baseline. Categorical endpoints will be presented in frequency tables with number and percentage of observations for each level.

12.2 Analysis Population

The following populations will be defined:

Intention-to-treat (ITT)	Includes all subjects who receive a test product. Subjects are analyzed based on the as treated principle.

Per protocol (PP) Includes all subjects in ITT who complete the study after pre-conditioning visit without any deviations that are considered to have substantial impact on the primary effectiveness outcome.

ITT is the primary population for all effectiveness and safety analyses. The primary effectiveness analysis will be repeated using the PP analysis set if there is at least a 10% difference in the number of subjects between the PP and ITT sets.

12.3 Demographics and Subject Characteristics

Demographic endpoints and subject characteristics will be presented based on the ITT analysis set using descriptive statistics, as appropriate.

12.4 Statistical Analysis Plan

Mean of the change from Baseline will be estimated at applicable post-Baseline timepoint. The null hypothesis, that the mean change from Baseline is zero, will be tested using methods described in Table 5. Statistical Analysis Plan~~Table 5. Statistical Analysis Plan~~.

The following will be calculated and reported for each parameter at applicable post-Baseline timepoint(s):

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

$$\text{Percent of subjects improved/worsened} = \frac{(\text{number of subjects improved/worsened from baseline})}{\text{total number of subjects}} \text{ x } 100$$

Table 5. Statistical Analysis Plan

Evaluation	Change from Baseline	Notes/Interpretation
Efficacy Grading • Skin smoothness (tactile) • Skin texture • Diaper dermatitis	Paired t-test; If normality fails, a Wilcoxon signed-rank test will be used.	A decrease in scores indicates an improvement
Tolerability Grading • Dryness • Peeling • Edema	Paired t-test; If normality fails, a Wilcoxon signed-rank test will be used.	A decrease in scores or lack of significant increase indicates tolerability/safety of the treatment product
Self-Assessment Questionnaire	N/A	Percentage of favorable and unfavorable responses will be provided for each question

Questionnaires will be tabulated; and the frequency and percentage of all response options will be reported for each question and time point. For questionnaire inquiries without baseline response data, a binomial (sign) test will be performed to test if the proportion of the combined designated favorable responses is equal to the combined designated unfavorable responses for each applicable question. A higher percentage of favorable responses with a significant *p* value indicates positive subject perceptions of the study treatment.

A more appropriate analysis may be performed, which will be recorded in biostatistics note to file and/or in the study report.

13. ADVERSE EVENTS

Throughout the course of the study, all adverse events will be monitored and reported on an adverse event CRF/eCRF without omitting any requested and known information. When AEs occur, the main concern is the safety of the study subjects. At time of the informed consent signature, each subject must be given the name and phone number of investigational site personnel for reporting AEs and medical emergencies.

At each visit, after the subject has had the opportunity to spontaneously mention any problems, the Investigator should inquire about AEs by asking the standard questions:

- "Has your child had any health problems since your last study visit?"
- "Have there been any changes in the medicines your child take since your last study visit?"

AEs should be reported for any clinically relevant change, as determined by the Investigator, in concomitant medication(s) that is the result of an untoward (unfavorable and unintended) change from baseline in a subject's medical health following exposure to the study treatment.

Changes from baseline in any protocol-specific parameter evaluated during the study are to be reviewed by the Investigator. In addition, the subject's responses to any questionnaire utilized during the study are to be reviewed by the Investigator. Any untoward (unfavorable and unintended) change from baseline in a protocol-specific parameter or question response that is clinically relevant, in the opinion of the Investigator, is to be reported as an AE. These clinically relevant changes will be reported regardless of causality.

13.1.1. Definition of an Adverse Event

An adverse event (AE) is defined as any untoward medical occurrence in a subject taking part in the clinical study, and which does not necessarily require a causal relationship with the investigational product and/or a clinical trial procedure.

An AE can be any unfavourable and unintended sign (including an abnormal laboratory value), symptom, or disease temporally associated with the use of the investigational product, whether or not related to this product.

When an AE has a likely or very likely causal relationship with the investigational product and/or a clinical trial procedure, it is named undesirable effect or related AE.

13.1.2. Local tolerability signs and symptoms (only applicable for cosmetic safety studies)

In cosmetic studies, local skin tolerability includes some expected functional and/or physical signs on the application area, observed by the Investigator or reported by the

subjects. Those signs are collected in the final report based on scales or a diary. If the severity of a local skin tolerability sign or symptom, is such that the product application is permanently discontinued and/or a corrective concomitant treatment (except moisturizer or emollient) is prescribed, it is recorded as an undesirable effect (related AE).

13.1.3. Definition of a Serious Adverse Event (SAE) and serious undesirable effect/related SAE

A serious adverse event (SAE) involves a serious injury that is life threatening, results in permanent impairment of a body function or permanent damage to a body structure or necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure, requires inpatient hospitalization or prolongation of an existing hospitalization.

Notes:

The term "immediate vital risk" refers to an event in which the subject was at risk of death at the time of the event; it does not refer to an event that hypothetically might have caused death if it was more severe.

Inpatient hospitalization is considered to have occurred if the subject has had to stay for a night at the hospital. Hospitalization solely for the purpose of a diagnostic test (even if related to an AE), elective hospitalization for an intervention that was already planned before subject enrolment in the clinical trial, admission to a day-care facility, social admission (e.g., if the subject has no place to sleep), or administrative admission (e.g., for a yearly examination) should not be considered as a SAE.

A serious undesirable effect/related SAE is defined as any SAE which the Investigator classifies as having a reasonable possibility for a causal relationship with the investigational product and/or the clinical trial procedure.

13.2 Severity Assessment

For all AEs occurring during the clinical trial, the Investigator is to classify and report the intensity of AEs using the following definitions as a guideline:

- Mild: awareness of signs and symptoms, but easily tolerated
- Moderate: discomfort, enough to cause interference with usual activity
- Severe: incapacitating, with inability to work or perform usual activity.

13.3 Causality Assessment

The Investigator is to assess the causal relationship (causality) between an adverse event and the investigational product and/or the clinical trial procedure according to the following definitions

(Decision of 25 November 2013 on Guideline on Annex I to Regulation (EC) No 1223/2009 (2013/674/EU) – Causality assessment of undesirable effect caused by cosmetic products):

- Very likely
- Likely
- Unlikely
- Excluded

Medical judgment should be used to determine the relationship, considering all relevant factors including the pattern of reaction, temporal relationships, positive de-challenge or re-challenge, relevant medical history, and confounding factors such as co-medication or concurrent diseases.

13.4 Collection, Management and Reporting Procedures

The period of collection of adverse events starts from the time of signature of the Informed Consent Form (ICF) by the subject until the end of the subject's participation in the clinical study.

If a Serious Adverse Event (SAE) is on-going at the final clinical trial visit, it should be followed by the Investigator until it has resolved or has reached a stable condition.

After the subject completes the clinical study, the Investigator should also inform the Sponsor (see Sponsor's contact details below) if he/she becomes aware of an SAE involving a subject who has participated in the clinical study.

At each post-enrollment visit, the Investigator will question the subject about AEs using an open non-persuasive question to elicit reporting of AEs, for example "*Have you noticed any change in your child's health since the last visit?*" Direct questioning and examination will be performed when appropriate.

The Investigator will obtain and maintain in the subject's files all pertinent medical records, and (if applicable) information and medical judgment from colleagues who assisted in the treatment and follow-up of the subject. If necessary, the Investigator will contact the subject's personal physician or hospital staff to obtain further details.

13.4.1. Management and reporting procedures for undesirable effects (i.e., related adverse events)

Undesirable effects should be recorded in the CRF in a summary table with at minimum the subject number, AE number, AE diagnosis or signs and symptoms, location, date of onset, seriousness, severity, action taken, relationship, date of resolution and concomitant treatment associated as well as a detailed narrative of the event.

In addition, based on his/her medical judgment, the Investigator will assess whether an undesirable effect requires immediate (i.e., within 24 hours) reporting to the Sponsor. In such cases, the summary table will be sent to the Sponsor, along with the AE narrative and any other relevant information (concomitant treatments, product weighing, …).

All undesirable effects should be appropriately documented, i.e., any relevant information such as demographics, medical history and concomitant therapies should be recorded in the CRF.

The Investigator is to monitor and record the progress of the adverse effect until the last subject's study visit.

The Investigator is to update the AE narrative as appropriate; each time follow-up information is collected and when the final outcome of the adverse effect is known.

13.4.2. Management and reporting procedures for Serious Adverse Events

The Investigator is to take the following steps:

1. Take prompt and appropriate medical action, if necessary. The safety of clinical trial subjects is the first priority

2. Ensure the AE is classified as an SAE. Immediately inform the Sponsor's representative of the event by email (see both contact details below) and discuss further actions to be taken:

   Global Vigilance email: safety.q-med@galderma.com
   US Vigilance email: pharmacovigilance.USDFW@galderma.com

3. Complete the Serious Adverse Event (SAE) form provided by the Sponsor's representative **Within 24 hours**, send by e-mail **to the Sponsor's representative** the completed SAE form, accompanied any other relevant information (e.g., test results or medical records).

4. Monitor, record and send to Sponsor's representative the progress of the event until it resolves or reaches a stable outcome, with or without sequelae (send the updated SAE form with follow-up information and any other relevant information to Sponsor's representative).

5. Obtain and maintain in the subject's file all pertinent medical records, information, and medical judgments from colleagues who assisted in the treatment and follow-up of the subject. If necessary, contact the subject's personal physician or hospital staff to obtain further details.

6. If applicable, comply with the regulatory requirement(s) related to the reporting of SAEs to the Institutional Review Board (IRB) / Independent Ethics Committee (IEC).

13.4.3. Anticipated Adverse Events for Sculptra

Information regarding anticipated AEs for *Sculptra* is included in the commercial IFU.

14. ETHICAL AND REGULATORY PROCEDURES

14.1 Research Standards/Good Clinical Practice

This study will be conducted in accordance with all applicable guidelines for the protection of human subjects for research as outlined in 21 CFR 50 the accepted standards for Good Clinical Practice (GCP), and the standard practices of SGS Stephens in accordance with the protocol and amendment(s) as applicable.

14.2 Quality Assurance/Audit/Inspection

To ensure compliance with GCP and all applicable regulatory requirements, Galderma Laboratories, L.P. may conduct a quality assurance audit of the site records, and the regulatory agencies may conduct a regulatory inspection at any time during or after completion of the study. The Investigator must agree to grant the auditor(s) and inspector(s) direct access to all relevant documents and to allocate their time and the time of their staff to discuss any findings/relevant issues.

14.3 Institutional Review Board

This study (protocol, ICF and all addenda) will be reviewed and approved by Sterling IRB. The study will not be activated and subjects will not be consented, receive any study products, or participate in any study procedures until the IRB has approved the protocol and the ICF. In addition, the IRB will review the study before any significant change in the protocol is initiated. After each review, the IRB's approval will be documented in a letter to the Investigator and a copy of the IRB approval letter will be forwarded to the Sponsor.

15. STUDY CONDUCT CONDISERATIONS

15.1 Clinical Monitoring

The conduct of the study will be closely monitored by representatives of Galderma Laboratories, L.P. following GCP, ICH guidelines, applicable SOPs, guidelines, and all local regulations. The clinical investigation will be monitored to ensure that: the rights and well-being of the subjects are protected; the reported data are accurate, complete and verifiable from applicable source documents; and the study is conducted in accordance with the currently approved protocol and any other study agreements, GCP, and all applicable regulatory requirements. The Investigator will allow the Galderma Laboratories, L.P. representatives to have access to all study records, CRF/eCRF, corresponding subject medical records, and any other documents considered source documentation. The Investigator also agrees to assist the representatives, if required, which can include AE reporting.

15.2 Study Deliverables

All study data and digital images will be forwarded to the Sponsor. Images will be labeled with study number, subject number, and timepoint.

15.3 Data Collection

Investigators must keep accurate records of all subjects' visits and all procedures done, being sure to include all pertinent study related information from which CRF/eCRF data will be recorded. Data for this study may be recorded in the subject's chart (e.g., source documents / electronic records) or if approved by the Galderma Laboratories, L.P. directly into CRF/eCRFs. If electronic records are maintained, the method of verification must be determined in advance of starting the study. The process of administering the informed consent must also be documented. Any and all side effects and AEs with the concomitant therapies associated must be thoroughly documented. Results of any diagnostic tests conducted during the study should be included in the source documentation. Pertinent telephone conversations with the subjects and/or Galderma Laboratories, L.P. concerning the study will be documented and kept on file.

It is required that the author of an entry in the source documents be identifiable. Direct access to all source documentation (medical records) must be allowed for the purpose of verifying that the data recorded in the CRF/eCRF are consistent with the original source.

Only designated individuals may complete the CRF/eCRFs. The principal Investigator will review the reported data and certify that the CRF/eCRFs are accurate and complete.

After monitoring has occurred at the clinical site(s) and the CRF/eCRFs have been reviewed, additional data clarifications and/or additions may be needed including AE reporting. Data clarifications and/or additions are documented and are part of each subject’s CRF/eCRFs.

15.4 Data Management

A double-entry method will be used to enter data captured on paper records into a spreadsheet database to ensure accurate data transfer, and any missing data and/or inconsistencies will be identified and corrected.

The self-assessment questionnaire will be completed by subjects electronically using HIPAA-compliant SurveyMonkey online survey software. Paper questionnaires may be completed if needed.

All images taken from the study will be saved and shared to the Sponsor via a data-protected platform.

15.5 Record Retention

The Investigator is required to maintain up-to-date, complete regulatory documentation as indicated by Galderma Laboratories, L.P. and the Investigator’s files will be reviewed as part of the ongoing study monitoring. The records must be easily accessible when needed (e.g., for a Galderma Laboratories L.P.’s audit or regulatory inspection) and must be available for review in conjunction with assessment of the facility, supporting systems, and relevant site personnel. Financial information is not subject to regulatory inspection and should be kept separately.

Galderma Laboratories, L.P. will inform the Investigator of the time period for retaining the site records in order to comply with all applicable regulatory requirements. The minimum retention time will meet the strictest standard applicable to a particular site, as dictated by local laws/regulations, Galderma Laboratories, L.P. SOPs, and/or institutional requirements.

The Investigator should take measures to prevent accidental or premature destruction of these documents. If the Investigator retires, relocates, or for other reasons withdraws from the responsibility of keeping the study records, custody must be transferred to a person who will accept the responsibility. Galderma Laboratories, L.P. must be notified in writing of the name and address of the new custodian.

15.6 Changes in Study Conduct/Amendments

No amendment will be done for modification(s) due to change in logistical or administrative aspect of the study (e.g., change in monitors, change of telephone numbers). In such a case, the appropriate institution(s) and/or person(s) will be notified of the changes.

Modification of the protocol is prohibited without prior written agreement in the form of a protocol amendment. All amendments will be created by Galderma Laboratories, L.P. and must be approved by the IRB prior to implementation except when required to mitigate immediate safety risks or when the changes involve only logistical or administrative revisions.

Amendments may necessitate that the informed consent and other study-related material be revised. If the consent form is revised, all Subjects/subjects currently enrolled in the study may be required by the IRB to sign the approved, revised informed consent form.

15.7 Confidentiality

All the data provided to the Investigator and his/her staff and all data obtained through this Galderma Laboratories, L.P. protocol will be regarded as confidential and proprietary in nature and should not be disclosed to any third party without Galderma Laboratories, L.P.'s written consent"

16. REFERENCES

1. Benitez Ojeda AB, Mendez MD. Diaper Dermatitis. [Updated 2023 Jan 31]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-.
2. Wesner E, Vassantachart JM, Jacob SE. Art of prevention: The importance of proper diapering practices. Int J Womens Dermatol. 2019 Mar 3;5(4):233-234. doi: 10.1016/j.ijwd.2019.02.005. PMID: 31700978; PMCID: PMC6831759.
3. Griffiths CEM, Wang TS, Hamilton TA, Voorhees JJ, Ellis CN. A Photonumeric Scale for the Assessment of Cutaneous Photodamage. Arch Dermatol. 1992;128(3):347–351. doi:10.1001/archderm.1992.01680130061006

APPENDIX I: INGREDIENT LISTS

HEALING OINTMENT

Active ingredient:

Petrolatum 71.5%

Inactive ingredients:

Cetearyl Ethylhexanoate
Butyrospermum Parkii (Shea) Butter
Beeswax
Microcrystalline Wax
Tocopheryl Acetate (Vitamin E Acetate)

APPENDIX II: SELF-ASSESSMENT QUESTIONNAIRE

Day 1

	Strongly agree 5	Agree 4	Neither agree nor disagree 3	Disagree 2	Strongly disagree 1
The product instantly soothes my baby's irritated skin	☐	☐	☐	☐	☐
I've noticed an instant relief on baby's irritated skin after applying the product	☐	☐	☐	☐	☐
My baby's skin feels smooth	☐	☐	☐	☐	☐
My baby's skin feels soft	☐	☐	☐	☐	☐

Visit 2 (Day 7 or Week 1)

	Strongly agree 5	Agree 4	Neither agree nor disagree 3	Disagree 2	Strongly disagree 1
The product does not feel greasy upon application	☐	☐	☐	☐	☐
My baby's skin feels softer and smoother	☐	☐	☐	☐	☐
The product soothes my baby's skin	☐	☐	☐	☐	☐
The product is easy to wipe/wash off without leaving any greasy residue	☐	☐	☐	☐	☐
The product lasts between diaper changes	☐	☐	☐	☐	☐
The product does not leave the skin feeling greasy	☐	☐	☐	☐	☐
This product is gentle on my baby's delicate skin	☐	☐	☐	☐	☐
This product has started to repair my baby's irritated skin	☐	☐	☐	☐	☐
This product provides a protective layer for my baby's skin	☐	☐	☐	☐	☐
I've noticed an immediate relief on my baby's skin after the product application	☐	☐	☐	☐	☐

Visit 3 (Day 21 or Week 3)

	Strongly agree	Agree 4	Neither agree nor disagree	Disagree 2	Strongly disagree 1

	5		3		
The product continuously protects my baby's skin from diaper rash	☐	☐	☐	☐	☐
The product provides long-lasting diaper rash relief	☐	☐	☐	☐	☐
Diaper rash flares are less frequent since starting this product	☐	☐	☐	☐	☐
Diaper rash flares are less intense since starting this product	☐	☐	☐	☐	☐
I have enjoyed using this product on my baby	☐	☐	☐	☐	☐
My baby's skin quality has improved since starting this product	☐	☐	☐	☐	☐
I love how this product leaves my baby's skin feeling soft and soothed	☐	☐	☐	☐	☐
My baby is less fussy since starting this product	☐	☐	☐	☐	☐
I worry less about my baby's diaper rash since starting this product	☐	☐	☐	☐	☐
My baby sleeps better since starting this product	☐	☐	☐	☐	☐

	Yes	**No**
I would continue using this product on my baby	☐	☐
I would purchase this product	☐	☐
I would recommend this product to other parents	☐	☐
I would switch from my current baby ointment to this product	☐	☐

Testimonials (please provide any comments on your experience, treatments, satisfaction/dissatisfaction, or anything related to this study)

_____

_____

_____