3M
Health Care
3M Center
St. Paul, MN 55144-1000

Clinical Study Protocol

Based on the International Conference on Harmonization
Good Clinical Practice
Consolidated Guideline
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Also Presented as
Guidance for Industry
E6 Good Clinical Practice:
Consolidated Guidance

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biological Evaluation and Research (CBER)
April 1996
ICH

Clinical Study Protocol

Study Number	EM-05-013620
Protocol Title	A Pilot Study Evaluating the Use of 3M™ Cavilon™ Advanced Skin Protectant in the Management of Damaged Skin Around an Ostomy, Drain, or Fistula
Principal Investigator	[redacted]
Sub-Investigator:	[redacted]
Research Facility	[redacted]
IRB	Western Institutional Review Board® (WIRB®) [redacted]
Sponsor	3M Health Care [redacted] St. Paul, MN 55144-1000
Sponsor Representative	[redacted]

[redacted]

3M Monitor (Delegate) [redacted]

3M Medical Monitor [redacted]

Approver List (3M Approvers Only):

Signer	Role	Date Signed
[redacted]		

[redacted]

[redacted]

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[redacted]

1. Protocol Synopsis

Study Title	A Pilot Study Evaluating the Use of 3M™ Cavilon™ Advanced Skin Protectant in the Management of Damaged Skin Around an Ostomy, Drain and/or Fistula
Study Product & Regulatory Status:	3M™ Cavilon™ Advanced Skin Protectant is a 510(k) cleared medical device.
Randomization	This is a pilot study with no randomization. Sample size: 30 (approximately 10 subjects with an ostomy, drain, or fistula.)
Study Objective(s) & Hypothesis:	Objective(s): The primary objective of this pilot study is to evaluate the feasibility, safety and efficacy of 3M™ Cavilon™ Advanced Skin Protectant when used in the management of damaged skin exposed to caustic body fluids from an ostomy, drain site or fistula.
Outcome Measures:	**Primary Efficacy Endpoint:** There are two primary endpoints. The first primary endpoint is the improvement of denuded skin (defined as clinical improvement from the baseline skin assessment) of the primary site of interest (ostomy, drain, or fistula). The second primary endpoint is a comparative pain score using the Faces Pain Visual Analog Scale comparing baseline to the end of study. [redacted]

[redacted]

Study Population:	**Inclusion/Exclusion Criteria:** Subjects may be enrolled into this study if the answers to all these questions are **yes**. 1. Is the subject 18 years of age or older? 2. Does the subject have red skin **with breakdown** (i.e. skin erosion and denudation or denudation of skin alone) at the **primary** site of an ostomy, drain and/or fistula? 3. Is the subject willing to have photographs taken of their skin and permit use of photographs in potential publication? 4. Is the subject willing to release rights to 3M for the use of the photos? 5. Is there a reasonable expectation that the subject will be in the hospital or available for follow-up visits during the 14 day study period? 6. Has the subject signed an Institutional Review Board-approved informed consent/assent document and authorized the use and disclosure of protected health information? Subjects are excluded from participation in this study if **any** of the answers to these following questions is yes. 1. If female, is the subject pregnant or breast feeding or has she given birth within the 3 weeks preceding the screening visit? 2. Does the subject have a known allergy to acrylates or cyanoacrylates? 3. Does the subject have a preexisting skin disease on the areas affected that may make skin assessments for this study difficult? 4. Does the skin area affected require treatment with a concomitant medication or product? 5. Has the subject received antifungal powders in the area affected within 24 hours prior to enrollment? 6. Has the subject received cyanoacrylate based skin protectant (such as Marathon) within 72 hours prior to enrollment? 7. Does the subject have any medical condition that in the opinion of the investigator should exclude him/her from participating in the study? 8. Has the subject been enrolled in any investigational study where product was applied to proposed study sites within 30 days of the screening visit?
Study Design:	Prospective pilot intervention study
Sample Size:	Maximum of 30 subjects
Geography:	Single site in USA over a period of up to 15 months
# Sites:	Estimated # of sites: 1 # of Subjects per site: up to 30 subjects

[redacted]

Assessments:	**Study Assessments:** • Subjects will be screened for the Inclusion/Exclusion criteria • History, demographics, and medications will be documented at baseline. • Subjects will remain in the study for up to 14 days following enrollment, receiving the product. Skin assessments will be performed on product dosing days. • Assessments will be done using a clinical skin assessment (described below) and photographs. • [redacted] • Subject's response regarding pain scores will be tracked following cleansing and product application. • Quantity of products used will be tracked.
Data Analysis Planned:	**Data Sets Analyzed:** • The primary efficacy data set will be the data set that will consist of subjects who have at least one skin assessment post-baseline. Dropouts will be censored at time of dropping out. **Efficacy Analysis:** • The primary response will be the percent change in area of epidermal loss between the areas observed at baseline subtracted from the area of epidermal loss at each time point. In addition, the time to re-epithelialization will be estimated using a Kaplan-Meier method. These will be summarized overall as well by each type of site (ostomy, drain, and/or fistula). • Pain scores assessed by the visual analog scale will be compared between baseline and each time point post-application of the barrier film. A paired t-test will be done to assess the significance of the change from baseline. These will be summarized overall as well by each type of damaged skin (ostomy, drain, and fistula). • [redacted] • [redacted] **Safety Analysis:** • Overall incidence of adverse events will be documented. The safety analysis data set will consist of all subjects enrolled in the study who received at least one application of the test material.

[redacted]

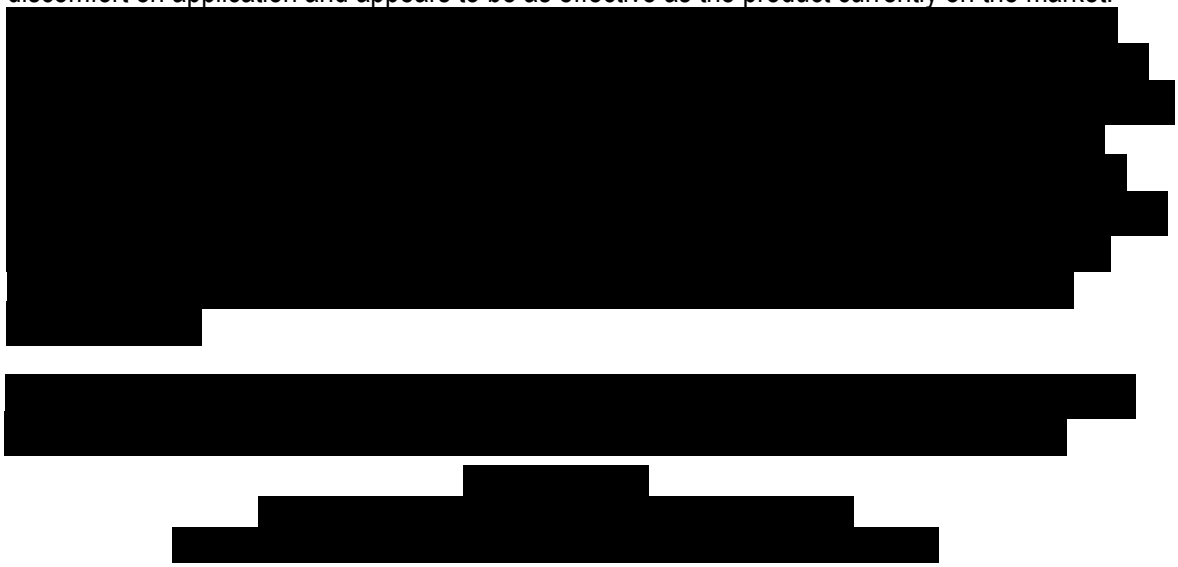
2. Background Information

The skin is the protective layer of the body and provides an important anatomical barrier to pathogens, irritants, water loss and environmental threats. Various conditions can damage the skin and breach integrity of the barrier. This can result in inflammation, disruption of epidermal integrity, pain and can increase the risk of infection.

Intact, dry skin, and containment of effluent with a well-fitted pouching system is imperative in the management of ostomies, high output fistulas, and leaking drain sites. When skin integrity is compromised, the cyclical pattern of pouch leakage/skin erosion/pouch leakage must be broken to enable epidermal resurfacing and restoration of an intact seal. Treatment of the skin relies on methods to create dry surfaces. Intact epidermis is maintained with skin barrier. Standard of care technique to ensure denuded skin is dry before applying a pouching system is called “crusting”. In this technique, the affected area is cleaned and dried. Dust stoma powder is applied over the affected tissue, with excess brushed away. The skin barrier is applied and allowed to dry, and may be repeated multiple times to provide a protective seal that allows the skin to re-epithelialize. If the area becomes contaminated with moisture, stool, urine, or wound drainage, the powder may become wet, necessitating that the process start over. This technique is time consuming and can be complex for some patients.

Standard of care techniques and products do not always appropriately resolve the situation at hand, or may take additional applications. However, newer approaches involve the formation of an adequate dry surface by the application of cyanoacrylate. It is applied to the irritated tissue, allowed to dry resulting in an immediate barrier film to form. Then the wafer or pouch is applied.
There is currently one skin protectant formula on the market to address partial thickness, moisture-associated skin damage secondary to ostomy, fistula, or drains. While this product is effective, patients frequently note pain or discomfort upon application.

3M™ Cavilon™ Advanced Skin Protectant is a new skin protectant formulated to protect damaged and denuded skin, even in the presence of exposure to the most potentially damaging body fluids, such as liquid stool and gastric fluid. The benefit of utilizing this product is that it does not cause discomfort on application and appears to be as effective as the product currently on the market.



[redacted]

This pilot study will examine the safety and efficacy of this novel technology to create an optimal environment where healing can occur by virtue of its ability to adhere to severely damaged or intact moist or wet skin, thus providing protection from liquid feces and other irritating body fluids. This study will also examine if this product is comfortable for subjects during application and wear. In addition, this product is easily cleaned and does not require frequent removal, making it more clinician friendly than paste barriers. If this product is equivalent to the current product while causing less discomfort upon application and throughout the use of the product, this may be an alternative option to offer patients.

3. Device Description and Regulatory Status

3M™ Cavilon™ Advanced Skin Protectant is a 510(k) cleared medical device. The product, and its use in the study, poses a non-significant risk to the participants, and intends to conduct the study under the abbreviated IDE requirements at 21 CFR §812.2(c). The device does not meet the requirements of a significant risk device since it is not an implant, not being used to support or sustain life, not being used for diagnosing, curing, mitigating, or treating disease, and does not present a potential for serious risk to health, safety, and welfare of a subject. The product is an acrylate polymer technology that utilizes cyanoacrylate(s) as a component of the formulation. This formulation is delivered from a non-stinging, rapid drying solvent. Upon application to the skin it forms a breathable, transparent coating.

3.1 Intended Use

Cavilon™ Advanced Skin Protectant forms a film barrier intended to protect intact or damaged skin. It is effective in conditions where skin is frequently or continuously exposed to moisture and caustic irritants such as feces, digestive fluids, wound drainage and urine. Cavilon™ Advanced Skin Protectant can also be used in areas exposed to friction and shear from bedding, clothing, shoes, or any other material that would rub against the skin.

4. Summary of Previous Studies

3M™ Cavilon™ Advanced Skin Protectant has been tested in a clinical pilot study, animal studies, and several healthy human volunteer studies including a durability study and a thermal pilot study. Summaries for these studies are included below.

4.1 Clinical Pilot Study

[redacted]

[redacted]

4.2 Animal Studies

[redacted]

4.3 Healthy Human Studies

[redacted]

4.4 Durability Study

The purpose of this study was to measure the durability, wear, and performance characteristics of [redacted]

4.5 Thermal Pilot Study

[redacted]

[redacted]

5. Study Objectives and Purpose

3M™ Cavilon™ Advanced Skin Protectant is a new skin protectant formulated to protect damaged and denuded skin even in the presence of exposure to the most potentially damaging body fluids, such as liquid stool and gastric fluid.

This pilot study will determine if 3M™ Cavilon™ Advanced Skin Protectant is effective for subjects with skin damage in areas exposed to caustic body fluids including ostomies, drains and fistulas. 3M™ Cavilon™ Advanced Skin Protectant can be used on multiple sites on a subject. The primary site **must** have red skin with breakdown (i.e. skin erosion and denudation or denudation of skin alone). Secondary sites can have red skin with or without breakdown.

5.1 Primary Objective

The primary objective of this pilot study is to evaluate the safety, feasibility, and efficacy of the product (3M™ Cavilon™ Advanced Skin Protectant) when used on damaged skin around an ostomy, drain or fistula.

6. Study Design

This is a pilot study evaluating the product, 3M™ Cavilon™ Advanced Skin Protectant, for the management of skin around an ostomy, drain and/or fistula. All subjects will receive the product for up to 14 days.

6.1 Randomization

This is a pilot study with no randomization.

6.2 Blinding

Blinding is not needed for a single product study.

6.3 Sample Size

A maximum of 30 subjects (10 subjects each for ostomy, drain and fistula) will be enrolled. A sample size of 30 is usually sufficient to estimate the distribution of a population and provide an estimate of performance for future studies.

[redacted]

6.4 Study Duration

In order to screen, enroll, and complete up to 30 evaluable subjects, an enrollment period of [redacted] is anticipated. 3M™ Cavilon™ Advanced Skin Protectant is indicated for application every 72 hours. Patient will return or be seen inpatient every 72 hours (±24 hours) for evaluation of product application. Assessment of denuded surface area will be measured at baseline, follow-up visits, and at the end of the study typically at day 14 but may be sooner if wound resolves at an earlier date. As previously noted, each subject may be followed for up to 14 days.

6.5 Primary Efficacy Endpoint

The primary endpoint includes the improvement in skin condition (denuded skin) at the primary site and pain score (using Faces Pain Visual Analog Scale) from baseline to the end of the study.

6.6 Secondary Efficacy Endpoints

[redacted]

6.7 Safety Endpoints

Assessment of the safety of the product will be based upon analyses of the number and percent of subjects with an adverse event (AE) and the nature of each AE. The data will be summarized based on the number and percent of subjects reporting AEs. In addition, AEs will be categorized and then summarized by relation to product and severity/intensity. Incidence of discontinuation will be summarized by reason for discontinuation.

7. Study Population

Subjects will meet the Inclusion/Exclusion criteria set forth in Section 7.1 and 7.2.A

7.1 Subject Inclusion Criteria

Subjects may be enrolled into this study if the answers to all these questions are **yes**.

1. Is the subject 18 years of age or older?
2. Does the subject have red skin with **breakdown** (i.e. skin erosion and denudation or denudation of skin alone) at the site of an ostomy, drain site, or fistula?
3. Is the subject willing to have photos taken of their skin and permit use of photographs in potential publication?
4. Is the subject willing to release rights to 3M for the use of the photos?
5. Is there a reasonable expectation that the subject will be in the hospital or available for follow-up visits during the 14 day study period?

[redacted]

6. Has the subject, signed an Institutional Review Board-approved informed consent/assent document and authorized the use and disclosure of protected health information?

7.2 Subject Exclusion Criteria

Subjects are excluded from participation in this study if **any** of the answers to these following questions is yes.

1. If female, is the subject pregnant or breast feeding or has she given birth within the 3 weeks preceding the screening visit?
2. Does the subject have a known allergy to acrylates or cyanoacrylates?
3. Does the subject have a preexisting skin disease on the areas affected that may make skin assessments for this study difficult?
4. Does the skin area affected require treatment with a concomitant medication or product?
5. Has the subject received antifungal powders in the area affected within 24 hours prior to enrollment?
6. Has the subject received cyanoacrylate based skin protectant (such as Marathon) within 72 hours prior to enrollment?
7. Does the subject have any medical condition that in the opinion of the investigator should exclude him/her from participating in the study?
8. Has the subject been enrolled in any investigational study where product was applied to proposed study sites within 30 days of the screening visit?

8. Subject Consent

The Investigator must ensure that written informed consent to participate in the study is obtained before including any individual as a subject in the study, and before conducting any study-related assessments. The Investigator must provide the prospective subject, with sufficient opportunity to consider whether or not to participate, and minimize the possibility of coercion or undue influence. The process is designed to 1) give the subject all the information that he/she needs, 2) ensure that the subject understands the information and 3) give the subject a chance to consider study participation. The process should permit the subject to ask questions and exchange information freely.

Specifically, the Investigator is to explain to each subject all elements of informed consent as specified in 21 CFR 50.25. This also includes explaining that photographs will be taken and may be used in publications in ways that do not identify the subject. After the explanation, the subject will voluntarily sign and date the consent/assent form if they wish to participate in the study. A copy of the consent/assent form must be provided to the subject. A signed and dated copy of the consent/assent form must be maintained in the Investigator Site File at all times. A sample consent form is provided in Appendix E. The informed consent process must be followed, and the subject's participation in the study, must be documented in the subject's medical record/chart.

8.1 Subject Authorization for Use & Disclosure of Protected Health Information (PHI)

Subjects will be consented using a current informed consent form that has been approved by the institutional review board (IRB). Subjects will be allowed adequate time to read the informed consent, discuss the consent with study staff and others (i.e. family members, friends, or any of their health care providers), and have their questions answered prior to signing the informed consent.

The subjects will be presented with the consent form in a private room and will be fully informed of the purpose, study related procedures, cost of the study, if they will be paid to be in the study, potential risks, potential benefits, alternative treatments, how long they are expected to participate, contact information and that participation is fully voluntary. Subjects will have the opportunity to have all questions answered to their satisfaction before signing the consent. The patients will be allowed to think about their participation prior to signing the informed consent form for as long as needed.

Signed informed consent for enrollment in this observational study will be obtained from eligible subjects by the PI, a Sub-I, or a member of the research team.

A copy of the signed Informed consent form will be given to the patient and will be scanned into the patient's medical record.

8.2 Subject Revocation of Authorization to Use & Disclose Personal Health Information

In order to implement a valid revocation of authorization, the subject must make the request in writing to Eastern Regional Medical Center, Inc. 1331 E Wyoming Avenue. Philadelphia. PA. 19124. The revocation cannot stop the use or disclosure of information that has been collected prior to the revocation, is needed to ensure complete and accurate study results, or is required by law or government regulation (e.g. reporting adverse events, etc.). Revocation of an authorization may not be used to withhold normal medical care from the subject, but will make the subject ineligible to receive study care.

8.3 Confidentiality of Data

The Principal Investigator will oversee the conduct of the study and all data will be kept confidential. Confidentiality will be maintained by using patient identification numbers instead of names. Consent forms, data collection sheets and records, linking a subject's name with their ID number will be maintained in a locked cabinet or locked office. Information to be stored on the computer will be identified by subject ID and will be password protected. Data disclosed outside the study team will be de-identified or will only include general group demographic information. Protected Health Information and/or identifiable study data will not be shared with anyone outside the study team or Health System, with the exception of the study sponsor, and federal regulators/ institutional officials for the purposes of auditing.

Subject medical information obtained by this study is confidential, and disclosure to third parties other than those noted below is prohibited.

Upon the subject's permission, medical information may be given to his or her personal physician or other appropriate medical personnel responsible for his or her welfare.

Data generated by this study must be available for inspection upon request by representatives of the U.S. FDA, national and local health authorities, the device manufacturer, and the IRB.

9. Screening and Enrollment

A representative from the site will complete the following screening and enrollment activities:

- **Obtain Informed Consent**
  - Explain the study to the subject, answer questions, and obtain written informed consent
- **Review the Inclusion/Exclusion Criteria**
- **Perform assessments required by the Inclusion/Exclusion criteria**
  - Collect urine sample and perform urine pregnancy test for female subjects who are of childbearing age. If the subject is post-menopausal, no pregnancy test is required.

If a subject does not meet all the Inclusion/Exclusion criteria, the subject will be excluded from the study.

If a subject meets all the Inclusion/Exclusion criteria, the Investigator, study nurse, or research staff (when appropriate) will complete the following remaining screening activities:

- **Record subject demographics.**
- **Obtain and record history.**
- **Obtain and record information describing current medications and treatment**
  - Oral or systemic medications prescribed by the subject's physician are allowed and will be noted on the appropriate CRF.
  - Use of moisture barrier, creams, ointments, pastes, or other topical medications in combination with the product are **not** allowed.
- [redacted]

10. Study Assessments

10.1 Study Product Application and Assessment-Initial and Follow-up Visits

Day 0 (Enrollment) - Initial product application and skin assessments
Week 1 (Day 3 ± 24 hours) - product application and assessment

[redacted]

Week 1 (Day 6 ± 24 hours) -product application and assessment
Week 2 (Day 9 ± 24 hours) -product application and assessment
Week 2 (Day 12 ± 24 hours) -product application and assessment
Day 14 (End of Study) – skin assessments will be completed at the final visit.
Unscheduled visits - product application and assessments will be completed if more product applications are needed due to leakage, skin irritation or standard of care.

Perform skin cleansing:
- Use plain tap water or normal saline which is standard practice
- Avoid rigorous scrubbing to minimize friction damage.
- Record pain score assessment using Faces Pain Scale Visual Analog

Conduct skin assessment for each site (the 4 inch x 4 inch area around the ostomy, drain, or fistula will be referred to as the "site" in this study)
- Complete a skin assessment:
  - Periwound skin condition
  - Percentage of site: normal skin, intact pink and/or red skin, epidermal loss
  - Presence of lesions
  - Signs of fungal infection

- **Study Product Application**
  - Following cleansing, the 3M™ Cavilon™ Advanced Skin Protectant will be applied
  - Apply 3M™ Cavilon™ Advanced Skin Protectant to the area surrounding the ostomy, drain or fistula (approximately 4 inches x 4 inches)
  - Use a new applicator of 3M™ Cavilon™ Advanced Skin Protectant for each type of site (ostomy, drain or fistula)
  - Record the number of applicators of the 3M™ Cavilon™ Advanced Skin Protectant used for each site (ostomy, drain or fistula)
  - Record pain score assessment using Faces Pain Scale Visual Analog during and after cleansing and application of the product (primary site only)
  - If there should be a need for product removal, use adhesive remover and gently wipe the area.
- **Take photographs (one photograph for each site after cleansing)**
  - Position the subject appropriately to take photos; one photo for each site the product is applied.
  - Take a photograph including the paper ruler in the photo (label paper ruler with patient information-patient number, date of visit, and site location)
  - Download photographs into the EDC system[redacted]
- **Medications**
  - Review and record changes to current medications.
- **Adverse Events**
  - Assess and record adverse events. Immediately report any Serious Adverse Event. (Refer to Adverse Event CRF instructions).
- **Additional Observation**

[redacted]

- Observe area for any signs of fungal infections

10.2 Final Study Visit

The subject's participation in this study is completed after 14 days of follow-up or last visit. At the final visit the following assessments will be completed:

- **Medications**
  - Review and record changes to current medications.
- **Adverse Events**
  - Assess and record adverse events. Immediately report any Serious Adverse Event. (Refer to Adverse Event CRF instructions).
- **Perform skin cleansing and record pain score using the Visual Analog Faces Pain Scale**
- **Take photographs (one photograph for each site after cleansing)**
  - Position the subject appropriately to take photos; one photo for each site the product is applied.
  - Take a photograph including the paper ruler in the photo (label paper ruler with patient information-patient number, date of visit, and site location)
  - Download photographs into the EDC system [redacted]
- **Conduct skin assessment for each site** (the 4 inch x 4 inch area around the ostomy, drain, or fistula will be referred to as the "site" in this study)
  - Complete a skin assessment:
    - Periwound skin condition
    - Presence of lesions
    - Percentage of site: normal skin, intact pink and/or red skin, epidermal loss
    - Signs of fungal infection
- [redacted]
- [redacted]
- **Documentation**
  - Complete and check all documentation.

[redacted]

10.3 Schedule of Events

Assessment	Screening / Enrollment Day 0	Week 1 Day 3 (± 24 hours)	Week 1 Day 6 (± 24 hours)	Week 2 Day 9 (± 24 hours)	Week 2 Day 12 (± 24 hours)	Unscheduled Visit (any time there is an issue with the site)	End of Study or Day 14
Informed Consent	X						
Inclusion/Exclusion	X						
Urine Pregnancy Test	X						
Demographics	X						
History & Current Product Use	X						
Medications	X	X	X	X	X	X	X
[redacted]	X						X
Skin Cleansing	X	X	X	X	X	X	X
Skin Assessment / scoring	X	X	X	X	X	X	X
Photographs	X	X	X	X	X	X	X
Product Application	X	X	X	X	X	X	
Adverse Events	X	X	X	X	X	X	X
[redacted]							X
Protocol Deviation	X	X	X	X	X	X	X

[redacted]

11. Subject Discontinuation

The Investigator may discontinue individual subjects from the study at any time. Subjects may voluntarily withdraw from the study at any time. The Investigator or study nurse will indicate on the appropriate CRF reason for, and date of, subject discontinuation.

Possible reasons for discontinuation are listed below:

- A subject develops a bacterial or fungal infection in the area included in the study or any other condition requiring the use of a topical treatment. Data collected up to the time where the subject required topical treatment will be analyzed.
- A subject develops any condition which, in the opinion of the Investigator, requires discontinuation from the study. If this condition is a suspected localized allergic reaction to the product, then appropriate testing confirmation should be performed and results/reports should be submitted to 3M. In addition, the event should be entered on the Adverse Event CRF.

The expectation is that subjects will be enrolled in this study for a period up to14 days. A subject who discontinues prior to their first assessment following product application, will be replaced with another qualified subject.

12. Subject Compliance

Subject compliance is not an issue in this study as subjects will not be applying the product themselves. CRFs will be used to monitor the number of cleansing episodes, and number of product application(s), performed by skilled care givers.

13. Study Supplies

13.1 Study Product

3M will label, package, and ship the investigational product to each research facility participating in the study. Each study product will be labeled with the following minimum information:

Study Number EM-05-013620

- 3M Health Care, St. Paul, MN 55144-1000
- 3M™ Cavilon™ Advanced Skin Protectant
- Lot number
- Package content: single-use applicator with ampoule
- Non-sterile Solution. Applicator is sterile if package is intact
- Use as directed in protocol. See Instructions for Use.
- **DANGER! HIGHLY FLAMMABLE!**
- Store at room temperature

[redacted]

- Expiration date

Instructions for Use (IFU) is provided in Appendix A.

13.2 Other Products

Other products supplied by the sponsor will contain a label indicating that these materials are for use in this study. Each commercial product supplied by the sponsor will be in the product's original commercial packaging.

The following materials will be provided:

- [redacted] Adhesive Remover Wipe

13.3 Photographic Equipment

3M will provide all photographic supplies necessary for the conduct of this study. Photographic instructions are included in Appendix D. A body diagram form will be included with the CRFs to identify primary and secondary sites. Label sites with P for primary and S for secondary. If multiple secondary sites, include number (e.g. S-1, S-2).

At the conclusion or termination of this study, the Investigator agrees to return all cameras and photographic materials, provided by 3M, in accordance with instructions provided by the study monitor.

13.4 Study Product

3M requires Investigators to maintain accountability and adequate inventory security of the product at all times. The Investigator or designee will:

- Upon receipt of product, check the contents and return the completed Confirmation of Release and Receipt of Clinical Supplies form to the sponsor's study monitor.
- Keep product in a secure storage area, accessible only to authorized individuals
- Dispense product only to subjects properly enrolled in the study
- Return all unused product to 3M at the end of the study, or dispose of as agreed upon.

14. Data Collection

14.1 Source Data

Case Report Forms (CRFs) will be provided for each subject. All required data will be recorded on the CRFs. Completed CRFs will be reviewed by the site monitor to ensure completeness and consistency and to ensure adequate quality control and assurance of subject data. Any discrepancies found during CRF review are to be clarified by the Investigator or designee.

The subjects' medical records will be the source data for medical history and current treatment regimen. Data collection forms will also be used. Data collection forms are source documents which must be retained by the Investigator such as the 3M Skin Condition Assessment. Information and data recorded on a data collection form must be accurately transcribed to the appropriate CRF.

[redacted]

Discrepancies between a medical record, or data collection form, and a CRF are to be resolved by the Investigator or designee.

The Investigator or designee must record all required subject data. An explanation must be documented for any missing data. The Investigator must attest that the data provided represents a complete and accurate record of each subject's participation in the study.

14.2 Computerized Systems

The following systems: [redacted] will be used to create, modify, maintain, archive, retrieve, transmit, analyze, and store data.

14.3 Case Report Forms

3M intends to use electronic data capture (EDC) software for this study. The site will be trained on the EDC software prior to study enrollment. The site will be provided with a manual, including instructions on how to complete the electronic CRFs and how to make CRF corrections. Data will be recorded on data collection sheets prior to data entry into the EDC, or will be entered directly into the EDC system. Once the forms are completed, the monitor will review the CRFs to ensure accuracy and completeness. The Investigator must review and sign the CRFs for each subject in a timely fashion following completion. Data for this study will be entered on the CRFs:

CRF	Screening & Enrollment	Days 1-14 or last visit	End of Study
[redacted]			
[redacted]			
[redacted]			
[redacted]			
[redacted]			
[redacted]			
[redacted]			
[redacted]			
[redacted]			
[redacted]			

[redacted]

15. Potential Risks and Benefits

15.1 Study Risks

The potential risks involved in this clinical study are considered to be consistent with those associated with similar skin protectant products used for the management and prevention of skin around ostomies/drains and fistulas. These risks include but are not limited to skin irritation.

15.2 Risk Minimization Actions

Additional risks may exist. Measures which have been taken to minimize risks include:

- The selection of Investigators trained in management and prevention of skin related issues around ostomies/drains and fistulas.
- Specific Investigator and study nurse training on the use of the product
- A well-defined clinical protocol, including specific inclusion/exclusion criteria, to enroll appropriate subjects in the study

Risks can be minimized at the clinical site through:

- Compliance with this protocol
- Performing assessments in the appropriate hospital environment
- Adherence to subject inclusion/exclusion criteria
- Close monitoring of the subject's status during follow-up

15.3 Anticipated Benefits

The potential benefit of this product is that it is able to attach to moist or wet, damaged skin forming an adherent, protective coating that creates an environment for healing. It will provide better skin protection of damaged skin against irritants such as gastric fluid or wound drainage. It will also allow adherence of a pouch.

Risk to Benefit Rationale

The study product is classified as non-significant risk. Based on data collected in previous studies, the risk-to-benefit ratio is within reason for foreseeable risks. However, appropriate observation and follow-up of subjects, will still be required as outlined in the protocol.

16. Safety Reporting

Adverse events will be collected for subjects beginning at Day 1 through the final study visit, or until the subject is discharged from the facility. An adverse event is any symptom, sign, illness, or experience, which develops or worsens during the course of the study, which may or may not be considered product related. The principal measures of safety will be the incidence of adverse events reported during the study.

An anticipated adverse event in this study is a skin reaction to the product itself. Worsening of the skin condition is expected in this subject population and would therefore not constitute an adverse event (related to the product being tested).

The Adverse Event CRF will be used to capture any safety-related concerns.

16.1 Adverse Events

The Investigator is responsible for identifying and reporting adverse events experienced by each subject throughout the study. An adverse event can occur at any time during the conduct of the study, in any phase of the study, or after the study is completed. An adverse event can be identified by the Investigator or reported by the subject.

Note: The Federal Privacy Rule (HIPAA) specifically permits the use and disclosure of protected health information "without written authorization of the individual" when used for public health activities such as reporting adverse events, tracking FDA-related products, enabling recalls, repairs, replacements, lookbacks, or conducting post-market surveillance [45 CFR 164.512]. This use and disclosure is subject to the *minimum necessary* standard, i.e. "the minimum necessary to accomplish the intended use, disclosure, or request" [45 CFR 164.502(b)(1)].

An adverse event is considered to be **serious** if it is:

- Life threatening of results in death
- Causes in-patient hospitalization
- Unduly prolongs hospitalization
- Persistently or significantly disabling
- A congenital anomaly
- Requires intervention to prevent outcomes above

Severity:

All adverse events will be classified as one of the following severities:

Mild: Subject is aware of signs or symptoms but they are easily tolerated.

Moderate: Signs or symptoms are sufficient to restrict but not prevent subject's daily activity.

Severe: Subject unable to perform daily activity.

Definitions:

- **Adverse event (AE)** means any undesirable clinical occurrence in a subject whether or not it is considered to be device related.

- **Device-related adverse event** (i.e. adverse device effect) is an AE considered by the Investigator to have a reasonable likelihood of being associated with the device.

- **Serious adverse device effect (SADE)** is a device effect that has a serious adverse effect on health or safety causing hospitalization or prolonged hospitalization, or is life threatening or causes death.

- **Unanticipated adverse device effect (UADE)** is any serious adverse device effect on health or safety or any life-threatening problem or death caused by, or associated with a device if that effect, problem or death was not previously identified in nature, severity or degree of incidence in the investigational plan or application, or any other unanticipated serious problem associated with a device that relates to rights, safety and welfare of subjects.

16.2 Adverse Event Recording and Reporting

All adverse events will be recorded on the Adverse Event CRF. The Investigator will record each product-related adverse event on an Adverse Device Effect Record. Event documentation will include the description, severity, seriousness, date of onset and resolution, relationship to the product, action taken, and outcome.

Relatedness:

Definitely related: Follows a reasonable temporal sequence from product application, and cannot be reasonably explained by known characteristics of the patient's clinical data.

Possibly related: Follows a reasonable temporal sequence from product application but could have been produced by the patient's clinical state regardless of the product.

Probably not related: Temporal association is such that the product is not likely to have had any reasonable association with the observed event.

Not related: No relationship to product is perceived.

The Investigator must promptly report an adverse device effect to the site monitor. If the adverse device effect is also considered by the Investigator to be serious and/or unanticipated, the Investigator must report it to the IRB as soon as possible and within IRB requirements.

A serious adverse event (SAE) involving a non-3M commercialized product is to be reported to the site monitor and the IRB.

If a subject has no adverse device effect during the study, the absence of such must be recorded on the CRF.

17. Statistics

17.1 Statistical Methods

17.1.1 Efficacy Analyses

[redacted]

The primary response will be the percent change in area of epidermal loss from baseline at each time point. In addition, the time to re-epithelialization will be estimated using a Kaplan-Meier method. These will be summarized overall as well by each type of site (ostomy, drain, or fistula). While no formal hypothesis testing is planned for this study, exploratory analyses will be performed which will include hypothesis testing.
Pain scores assessed by the visual analog scale will be compared between baseline and each time point post-application of the barrier film. A paired t-test will be done to assess the significance of the change from baseline. If subjects are unable to rate the pain (e.g. if the subject is comatose), their data will not be included in this analysis. These will be summarized overall as well by each type of damaged skin (ostomy, drain, or fistula).

[redacted]

Skin condition data from the secondary sites will also be summarized for each type of site (ostomy, drain, and/or fistula).

17.1.2 Safety Analyses

The incidence of adverse events will be summarized overall as well by each type of damaged skin (ostomy, drain, or fistula).

17.2 Sample Size Justification

This is an observational study with a maximum of 30 subjects enrolled with either an ostomy, drain, or fistula.

17.3 Interim Analyses and Criteria for Termination of the Study

There is no interim analysis planned for this study.

17.4 Procedures for Accounting for Missing, Unused, and Spurious Data

The Kaplan-Meier estimate of time to healing of skin will censor any missing data due to subjects completing the study early. Any other missing data will be documented, and decisions on the use of the data will be documented in the Statistical Analysis Plan.

17.5 Deviations to Statistical Plan

Any deviations to the statistical analysis will be documented in the Statistical Analysis Plan prior to final analysis.

[redacted]

18. Protocol Modifications

18.1 Protocol Amendments

The party initiating an amendment must confirm it clearly in writing using the Amendment/ Administrative Revision form. It must be signed and dated by 3M and, in the case of a significant amendment, the Investigator. A significant amendment means one that affects the safety, rights or welfare of subjects, the scope of the investigation, or the scientific quality of the study.

3M will submit significant protocol amendments to the Investigator for submission to the IRB. 3M will also notify the Investigator when a protocol amendment may be implemented.

18.2 Protocol Deviations

A protocol deviation is a departure from the protocol that will likely affect the safety, rights or welfare of subjects, the scope of the investigation, or the scientific quality of the study.

A protocol deviation is only for an individual subject. Protocol deviations are documented on a Protocol Deviation **CRF**.

Deviations that potentially affect 1) subject safety, rights or welfare, 2) data integrity or 3) compromise the statistical analysis of the study require immediate communication to 3M. Each protocol deviation will be documented by completing a Protocol Deviation CRF. This documentation will include the type of deviation and a description of the circumstances surrounding the deviation.

Deviations which are made to protect the life or physical well-being of a subject in an emergency must be reported to the IRB [redacted]

19. Compliance

This study will be conducted in accordance with the relevant parts of the ICH Guidelines for Good Clinical Practices, ethical principles that have their origins in the Declaration of Helsinki, and FDA 21 CFR Part [redacted]. The study shall not begin until the required IRB approval has been obtained. The IRB will review all appropriate investigational documentation in order to safeguard the rights, safety and well-being of subjects. The study will only be conducted at sites where IRB approval has been obtained. The clinical protocol, informed consent, written information given to the subjects, safety updates, progress reports, and any revisions to these documents, will be provided to the IRB by the Investigator. Any additional requirements imposed by the IRB shall be followed, if appropriate.

20. Investigator Responsibilities

The Principal Investigator of a clinical site is responsible for ensuring that the study is conducted in accordance with the Clinical Study Agreement, the protocol, ICH guidelines for Good Clinical Practice, FDA 21 CFR Part [redacted], ethical principles that have their origins in the Declaration of

[redacted]

Helsinki, any conditions of approval imposed by the reviewing IRB, whichever affords the greater protection to the subject.

The Principal Investigator's responsibilities include, but are not limited to, the following:

- Prior to beginning the study, sign the Investigator Agreement and Protocol Signature page documenting his/her agreement to conduct the study in accordance with the protocol.
- Make no changes in or deviate from this protocol, except to protect the life and physical well-being of a subject in an emergency; document and explain any deviation from the approved protocol that occurred during the course of the clinical study.
- Create and maintain source documents throughout the clinical study and ensure their availability with direct access during monitoring visits or audits; ensure that all clinical study-related records are retained per requirements.
- Ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports.
- Record, report, and assess every adverse event.
- Report to the IRB any SAEs, and supply 3M with any additional information related to the safety reporting of a particular event.
- Maintain the product accountability records and control of the product, ensuring that the study product is used only by authorized/designated users and in accordance with this protocol and Instructions for Use.
- Allow 3M or designee to perform monitoring and auditing activities, and be accessible to the monitor and respond to questions during monitoring visits.
- Allow and support regulatory authorities and the IRB when performing auditing activities.
- Ensure that informed consent is obtained in accordance with this protocol and local IRB requirements.
- Inform the subject of any new significant findings occurring during the clinical study, including the need for additional medical care that may be required.
- Ensure that clinical medical records are clearly marked to indicate that the subject is enrolled in this clinical study.
- Ensure that the center facilities and study team are adequate and are maintained and documented for the duration of the clinical study.

20.1 Delegation of Responsibility

When specific tasks are delegated by an Investigator, [redacted] the Investigator is responsible for providing appropriate training and adequate supervision of those to whom tasks are delegated. Delegation of responsibilities will be assigned and recorded on the Delegation of Authority Log. Any changes to responsibilities must be

[redacted]

approved by the Investigator. The Investigator is accountable for regulatory violations resulting from failure to adequately supervise the conduct of the clinical study.

20.2 Institutional Review Board

This protocol, the informed consent document, and relevant supporting information must be submitted to the IRB for review and must be approved before the study is initiated. Prior to gaining approval to enroll subjects in the study, the clinical site will provide 3M with documentation verifying that their IRB is registered. The study will be conducted in accordance with U.S. FDA, applicable national and local health authorities, and IRB requirements.

A copy of the written IRB approval of the protocol and Informed Consent Form, must be received by 3M before recruitment of subjects into the study and shipment of the product. Prior approval must also be obtained for other materials related to subject recruitment or which will be provided to the subject.

Annual IRB approval and renewals will be obtained throughout the duration of the study as required by the IRB. Copies of the Investigator's reports, and the IRB continuance of approval, must be provided to 3M.

The Principal Investigator is responsible for keeping the IRB apprised of the progress of the study and of any changes made to the protocol as deemed appropriate, but in any case the IRB must be updated at least once a year. The Principal Investigator must also keep the IRB informed of any significant adverse events.

Investigators are required to promptly notify their respective IRB of all adverse events that are both serious and unexpected. IRB may have other specific adverse event requirements that investigators are expected to adhere to. Investigators must immediately forward to their IRB any written safety report or update[redacted]..

21. Data Handling and Record Keeping

21.1 Study Personnel

Prior to study initiation, the Investigator must provide 3M with a signed Investigator Agreement (Statement of Investigator). The Agreement contains pertinent Investigator information (e.g. qualifications, experience, etc.) as well as the Investigator's commitment to conduct the study according to the protocol and all applicable state and federal regulations.

21.2 Pre-Study Documentation Requirements

Prior to study initiation, the Investigator must provide 3M with the following documents:

- Signed protocol including any amendments in place prior to study initiation
- Curriculum vitae for the Investigator and any Sub-Investigators
- IRB approved consent form

[redacted]

- HIPPA authorization form
- IRB study approval letter
- IRB name, location and chairperson
- Financial Disclosure documents per 21 CFR 54
- Signed Clinical Study Agreement

21.3 Records Retention

The Principal Investigator or the clinical site will maintain, at the site, in their original format all supporting study documents and source documentation for data collected on study subjects.
The Investigator will maintain the required study records during the investigation and for a minimum of 2 years after the latter of the following two dates: The date on which the study is terminated or completed, or the date the records are no longer required for purposes of supporting a regulatory submission.
Records that must be maintained by the Investigator include, but are not restricted to:

- Signed study protocol, amendments, deviations
- IRB approval of protocol, consent form, authorization form*, waiver of consent and/or authorization and amendments to any of these documents
- Applications to the IRB
- Signed consent and authorization forms
- Case report forms
- Adverse event reports
- Records of receipt, use or disposition of the study product
- Correspondence relating to the study
- Investigator brochure
- Financial disclosure documents
- Sponsor Final Report

21.4 Records Custody

If the Investigator withdraws from the study, or relinquishes his/her responsibility for maintaining these essential documents, custody must be transferred to an individual who will assume responsibility and 3M must receive written notification of the custodial transfer.

21.5 Final Report

3M will prepare and submit a Sponsor Final Report to all reviewing IRBs [redacted] after study completion or termination.

22. Clinical Monitoring

3M, as sponsor of this study, is responsible for ensuring the proper conduct of the study with regard to protocol adherence and validity of the data recorded on the CRFs [redacted] Monitoring will be performed during the study to assess continued compliance with the protocol and applicable regulations. In addition, the site monitor will verify that study records are adequately maintained, and that data are reported in a satisfactory manner with respect to timeliness, adequacy, and accuracy, and that the Investigator continues to have sufficient staff and facilities to conduct the study safely and effectively.

[redacted]

22.1 Source Documents

The Investigator will give the site monitor direct access to source documents that support data entered on the CRFs and make available such records to authorized 3M, quality assurance, IRB, and regulatory personnel for inspection and/or copying.

Note: The Federal Privacy rule (HIPAA) specifically permits the use and disclosure of protected health information "to a person subject to the jurisdiction of the Food and Drug Administration (FDA) [e.g. study sponsor] with respect to an FDA-related product or activity for which that person has responsibility, for the purpose of activities related to the quality, safety, or effectiveness of such FDA-regulated product or activity" [45 CFR 164.512(b)(1)(iii)].

22.2 Monitoring Plan

A monitoring plan will be developed prior to the initiation of the study, which outlines the extent and nature of monitoring appropriate for the clinical study, including the frequency of visits and the strategy for source data verification, based on considerations such as the objective, design, complexity, size, critical data points, and endpoints of the clinical study.

22.3 Audits

The study may be subject to a quality assurance audit by 3M, or its designees, as well as inspection by appropriate regulatory authorities. It is important that the Investigator and relevant study personnel are available during on-site monitoring visits or audits and that sufficient time is devoted to the process.

23. Quality Control and Quality Assurance

3M is responsible for implementing and maintaining quality assurance and quality control systems through written standard operating procedures (SOPs) to ensure that this study is conducted and data are generated, documented and reported, in compliance with the protocol, GCP and regulations. Study monitoring is carried out to accomplish this.

24. Ethical Considerations

This study will be conducted in accordance with the principles that have their origin in the Declaration of Helsinki, 21 CFR 50 (Informed Consent) and 56 (IRBs). The study will start only after approval of the protocol and consent form by the IRB. The approval letter or notice must contain the IRB name and identification number, meeting date, and sufficient information to identify the protocol and informed consent by name and number that were reviewed. 3M, prior to study initiation, must receive a copy of the IRB approval letter.

3M does not consider 3M™ Cavilon™ Advanced Skin Protectant to be a significant risk device. This study will be conducted in compliance with this protocol, GCP and applicable state and federal regulations including 45 CFR 160 & 164 (Authorization for Use/Disclosure of PHI),21 CFR 812.2 [c

(cleared 510(k) device regulations , 50 (Informed Consent), 56 (IRBs), and 54 (Financial Disclosure) for studies included in a 510(k).

25. Study Termination

Conditions that may warrant termination of the study by 3M include, but are not limited to, the following:

- The discovery of an unexpected, serious, or unreasonable risk to study subjects.
- Failure of the Investigator to comply with pertinent FDA regulations.
- Insufficient adherence to protocol requirements.
- Failure of the Investigator to enroll subjects into the study at an acceptable rate.
- Failure of the Investigator to comply with either pertinent FDA regulations or federal (e.g. HIPAA) and state privacy regulations.
- Submission of knowingly false information from the Investigator to 3M.
- Withdrawal of IRB approval.
- A decision on the part of 3M to suspend or discontinue evaluation of the product.

3M or the Investigator has the right to discontinue the study at any time for medical and/or administrative reasons. This should occur as soon as possible, after mutual agreement.

26. Publication Policy

In accordance with 3M's corporate policy, the company requires disclosure of its involvement as a sponsor or financial supporter in any publication or presentation relating to a 3M study or its results.

27. References

[1]Milne CT, Saucier D, Trevellini C, & Smith J. Evaluation of a cyanoacrylate dressing to manage peristomal skin alterations under ostomy skin barrier wafers. *Journal of Wound, Ostomy & Continence Nursing*, 2011; 38 (6):676-679.

[redacted]

APPENDIX A- Instructions for Use of 3M™ Cavilon™ Advanced Skin Protectant

3M™ Cavilon™ Advanced
Skin Protectant

Product Description:

3M™ Cavilon™ Advanced Skin Protectant is a polymeric-cyanoacrylate solution intended for the protection of intact or damaged skin. Upon application to skin, the liquid dries rapidly to form a primary long-lasting waterproof, highly durable film barrier. It is elastomeric, adhering to the contours of the skin and providing a uniform film. The film is transparent and possesses good oxygen and moisture vapor permeability.

The polymer-cyanoacylate is dispersed in a non-stinging solvent. The film is colorless, non-cytotoxic and has a low dermatitis potential. The film adheres to dry, moist or wet skin surfaces and remains intact during conditions of continuous or repeated exposure to moisture or caustic irritants. It will wear off the skin and does not require removal.
.

Ingredients: Hexamethyldisiloxane, Acrylic Tetrapolymer, 2-Octyl Cyanoacrylate

Indications for Use

Cavilon™ Advanced Skin Protectant forms a film barrier intended to protect intact or damaged skin. It is effective in conditions where skin is frequently or continuously exposed to moisture and caustic irritants such as feces, digestive fluids, wound drainage and urine. Cavilon™ Advanced Skin Protectant also can be used in areas exposed to friction and shear from bedding, clothing, shoes or any other material that would rub against the skin.

Contraindications

Cavilon Advanced Barrier Film is NOT to be used:

- as a wound dressing for full thickness wounds
- in or around the eyes

Warnings

1. **DANGER! EXTREMELY FLAMMABLE!**
2. Cavilon Advanced Skin Protectant is extremely flammable until it has completely dried on the skin.

[redacted]

3. Cavilon Advanced Skin Protectant should only be applied when no ignition sources or heat-producing devices are in use.

4. Avoid using Cavilon Advanced Skin Protectant around flames.

5. Use Cavilon Advanced Skin Protectant only in well ventilated area.

6. Avoid use on individuals who are allergic to any of the ingredients.

7. The product is individually packaged for single use only. Reuse could result in increased risk of infection, or inadequate product performance.

8. Cavilon Advanced Skin Protectant is not intended for applications requiring sterile product (e.g. infusion catheter site protection and care or surgical site protection).

9. Keep out of the reach of children.

Precautions

1. Skin absorption and the effectiveness of topical medications (including: antimicrobials, antifungals, and analgesics) may be reduced or prevented by the presence of the Cavilon Advanced Skin Protectant.

2. Use of other barrier products, ointments, creams or lotions may significantly reduce the effectiveness of the product.

3. The product can increase the adhesion of some adhesive products.

Directions for Use

1) Cleanse skin before applying Cavilon Advanced Skin Protectant. Gently dry areas of intact skin. If areas of erosion (denudement) are present, excess serous or serosanguinous drainage may be blotted with a gauze pad if necessary.

2) Grasp applicator and place thumb at the end of the lever. Aim the sponge end of the applicator downward and firmly depress the lever to break the internal ampule. (Figure 1) A snapping or popping noise will be noted as the ampule breaks.

[redacted]

Figure 1

3) Keep the applicator pointed in a downward position for approximately 10 seconds. Fluid will flow into the foam sponge; continued pressure on the lever is not required. Fluid will not completely saturate the sponge to the edges.

4) Using an even, sweeping motion, gently wipe the foam sponge across the skin (Figure 2); downward pressure on the applicator is not needed and may result in pooling of fluid. Move to adjacent unprotected area and repeat application until the entire area of concern has been covered.

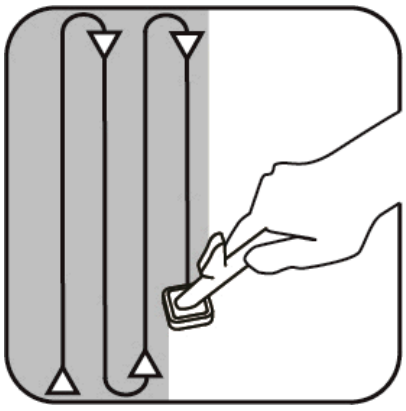


Figure 2.

Apply Cavilon Advanced to *all* skin that is exposed to stool and/or urine, or irritating body fluid. Allow the area to dry for 30 seconds.

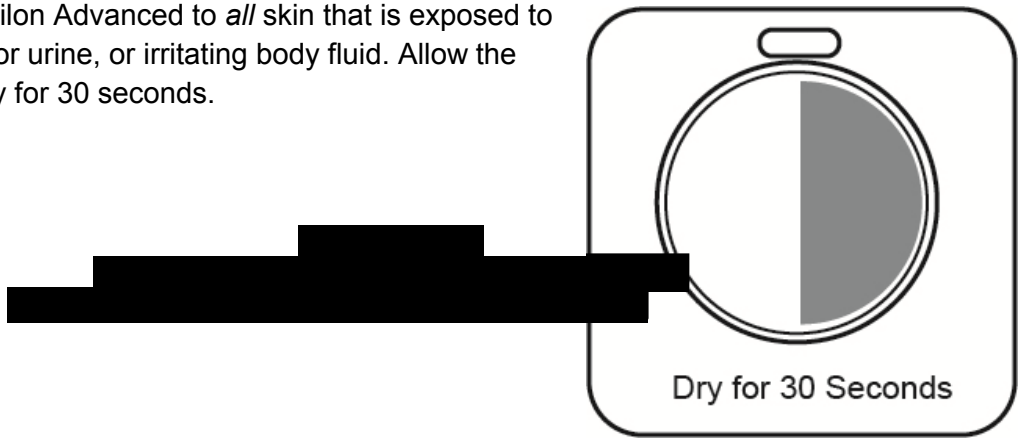


Figure 3

If an area is missed, wait until the fluid has dried completely before applying additional product.

5) If Cavilon Advanced Skin Protectant is applied within a skin fold or other area of skin-to-skin contact, make sure that the skin surfaces are separated to allow the fluid to dry completely (30 seconds) before allowing skin to return to the normal position.

6) When used under adhesive tapes, dressings, or devices allow Cavilon Advanced Skin Protectant to dry for approximately 1 minute before covering with adhesive products. Refer to Precaution Statement # 3.

7) Cleanse affected area as needed. Cavilon Advanced Skin Protectant is waterproof and is not removed by cleansing.

8) Removal is not required. If desired, the film can be removed with an adhesive remover containing hexamethyldisiloxane (HMDS).

9) Reapply two to three times per week. More frequent application may result in buildup of the product.

Storage/ Shelf Life/Disposal

For best results, the product should be stored in a cool and dry environment. Avoid excessive heat.

For shelf life, refer to the expiration date on each package.

Refer to facility policy for disposal.

How supplied

Applicators are individually packaged for single patient one time use only. The solution is non-sterile. The applicator is sterile if package is intact. Do not use if the package is damaged or opened.

[redacted]

APPENDIX B – [redacted]

[redacted]

APPENDIX C – CRFs

[redacted]

APPENDIX D – Photographic Instructions

[redacted]

APPENDIX E – Informed Consent

[redacted]

[redacted]