Clinical Study

Title of the Clinical Study	Effects of an advanced skin protectant in the management of incontinence-associated dermatitis compared to hospital standard care practice: an exploratory randomized controlled trial
Coordinating Investigator	[redacted] Charité – Universitätsmedizin Berlin [redacted] Charitéplatz 1 10117 Berlin Germany [redacted]
Investigators United Kingdom	[redacted] University Hospital Southampton Southampton SO16 6YD United Kingdom [redacted] Co-Investigator: [redacted] University of Southampton [redacted] Southampton SO16 6YD United Kingdom [redacted]

Investigator
Belgium

[redacted]
Universitair Ziekenhuis Gent
De Pintelaan 185
9000 Gent
Belgium
[redacted]
Co-Investigator (Researcher):
[redacted]
UZ Gent [redacted]
De Pintelaan 185
9000 Gent
Belgium
[redacted]

Investigator
Germany

[redacted]
Charité – Universitätsmedizin Berlin
[redacted]
Charitéplatz 1
10117 Berlin
Germany
[redacted]

Blinded Assessor
Photography

[redacted]
UZ Gent [redacted]
De Pintelaan 185
9000 Gent
Belgium
[redacted]

Sponsor	3M Deutschland GmbH Carl-Schurz-Str. 1 41453 Neuss Germany Web: http://www.3mdeutschland.de
3M Biostatistician	[redacted] 3M Center, 270-3A-04 St. Paul, MN 55144-1000 USA [redacted] [redacted] Web: http://www.3m.com
3M Monitor	[redacted] 3M Deutschland GmbH Carl-Schurz-Str. 1 41453 Neuss Germany [redacted] Web: http://www.3mdeutschland.de
3M Medical Monitor	[redacted] 3M Deutschland GmbH Carl-Schurz-Str. 1 41453 Neuss Germany [redacted] Web: http://www.3mdeutschland.de
CRO	acromion GmbH Europaallee 27-29 50226 Frechen Germany [redacted] Web: http://www.acromiongmbh.com/

Approver List (3M Approvers Only):

Signer	Role	Date Signed
[redacted]	Clinical	January 30, 2018 02:06:51 AM CST
[redacted]	Clinical	January 29, 2018 10:38:52 AM CST
[redacted]	Clinical	January 30, 2018 03:01:46 AM CST
[redacted]	Regulatory	January 30, 2018 07:29:50 AM CST

Table of Contents

Abbreviations

AE	Adverse Event
ADE	Adverse Device Effect
eCRF	Electronic Case Report Form
CRO	Contract Research Organization
EC	Ethics Committee
eDC	Electronic Data Capture
EEC	European Economic Community
EPUAP	European Pressure Ulcer Advisory Panel
FDA	Food And Drug Administration
GCP	Good Clinical Practice
GLOBIAD	Ghent Global IAD Categorization Tool
IAD	Incontinence-Associated Dermatitis
ISO	International Organization for Standardization
IC	Informed Consent
IFU	Instructions For Use
NPUAP	National Pressure Ulcer Advisory Panel
n	Number
p	Probabiltiy
PU	Pressure Ulcer
RCT	Randomized Controlled Trial
SAE	Serious Adverse Event
SAS	Statistical Analysis System
SOP	Standard Operating Procedure
UK	United Kingdom
USA	United States of America

1. Overall synopsis

Study Title	Effects of an advanced skin protectant in the management of incontinence-associated dermatitis compared to hospital standard care practice: an exploratory randomized controlled trial
Sponsor	3M Deutschland GmbH Carl-Schurz-Str. 1 41453 Neuss Germany
Study Design	Exploratory, randomized, controlled, multi-center, multi-country
Study Device & Regulatory Status	3M™ Cavilon™ Advanced Skin Protectant CE-marked medical device class IIa according to the Medical Device Directive 93/42/EEC, Annex IX, rule 4
Comparator	Local hospital IAD care regime (IAD care products and procedures)
Study Objective(s) & Hypothesis	The intention of the study is to assess the effects of 3M Cavilon Advanced Skin Protectant in comparison to different local IAD care regimes in hospitals. The study is designed as an exploratory study to learn more about the effect size of certain variables such as healing outcome when compared to different local IAD care regimes and will consider the medical routine of Western European hospitals regarding IAD care under real-world circumstances. Due to the exploratory design no formal a priori hypothesis is defined. The results of the study will be used to examine the feasibility of a potential subsequent confirmatory RCT.
Study Endpoints	3M Cavilon Advanced Skin Protectant compared to local hospital IAD care • Number and percentage of patients completely healed (skin free of any IAD signs, including erythema) • Number and percentage of patients improved with regard to IAD category • Number and percentage of patients with 100% re-epithelialization of skin loss (skin loss: skin is moist, as the epidermal layer is missing) • Time to complete healing or reduction in IAD category • Protection of IAD category 1 patients from developing IAD category 2 • Prevention with regard to IAD recurrence • Material cost based on product utilization such as type of products, frequency of application and days of treatment • Use of resources involved in the IAD therapy • Nursing time to clean up incontinence and to administer IAD treatment products • Pain scores with regard to cleansing procedure and application of IAD product (Wong-Baker FACES® Pain Rating Scale: assessment only for cognitively healthy patients according to the judgement of the study nurse) • Number and percentage of patients with adverse events and the nature of each adverse event as defined for this study

Study Population	Hospitalized incontinent patients with IAD category 1A or 2A according to the Ghent Global IAD Categorization Tool (GLOBIAD). IAD category 1A: Persistent redness without clinical signs of infection IAD category 2A: Skin loss without clinical signs of infection
Study Area	Study Area: The study area is defined as the sacral region going down to the upper thighs, bordered approximately 5 cm below the gluteal fold. The study area is to be photographed on Day 01 and every three days until the end of the study (Day 04, 07 … Day 21). Additional photos are to be taken at the first day no evidence of IAD is present (transition from IAD1 to IAD free) and if applicable, on the first day of 100% re-epithelialization of skin loss (transition from IAD2 to IAD1). The central reader will conduct a blinded skin assessment based on the photo documentation of the study area on Day 01, first day(s) of transition to an improved IAD category and on the last day of patient's study participation.  Study Area: IAD has to be present in this zone Skin Assessment: The patient's skin will be assessed daily for IAD signs in the study area and additionally the navel to upper thigh region according to the GLOBIAD criteria. Futhermore, an estimate will be provided for the total affected IAD area including signs of erythema and in addition with focus on skin loss only, if applicable.  Skin Assessment Areas: Back Side & Front Product Application: Cavilon Advanced Skin Protectant will be applied to the study area that is defined as the sacral region going down to the upper thighs, bordered approximately 5 cm below the gluteal fold (IAD affected as well as unaffected skin). The genital area and the frontal skin folds will be treated only in case of visible IAD and only for the IAD affected skin. In consideration of the manufacturer's instruction for use no topical medication or other product shall be applied on top of the barrier film because the effectiveness of either film or medication might be reduced. The hospital standard care products of the comparator group will be applied to the skin areas following the local hospital ward procedures and considering the manufacturers' instructions for use especially with regard to contraindications. The use of topical medication or product other than the IAD treatment is not allowed for the study area in the comparator group.

Inclusion Criteria	Patients may be enrolled into this study if the answers to all these questions are yes. 1. Is the patient 18 years or older? 2. Has the patient or their legally authorized representative signed the Informed Consent Form? 3. Does the patient have IAD category 1A or IAD category 2A in the study area? 4. Is the patient incontinent and does stool and/or urine come into direct contact with the skin? 5. Is the patient able to be turned/positioned with regard to skin assessment and photo documentation? 6. Is there a reasonable expectation that the patient will remain in the hospital setting for at least 7 days?
Exclusion Criteria	Patients are excluded from participation in this study if any of the answers to these questions are yes. 1. Is the patient pregnant or breast feeding? 2. Does the patient have a known hypersensitivity or allergy to acrylate or cyanoacrylate? 3. Does the patient have a stage II, III, IV or unstageable pressure ulcer or other suspected deep tissue injury in the study area? 4. Does the patient require topical treatment due to a fungal, bacterial or viral infection in the study area? 5. Does the patient require treatment with topical medication or product other than the IAD treatment in the study area? 6. Does the patient have any other local dermatological disease or skin condition interfering with this study? 7. Does the patient have any medical condition (e.g. end of life, planned elective surgery) that in the opinion of the investigator should exclude him/her from participating in the study? 8. Does the patient participate in another study with a known or implied effect on skin barrier function?
Withdrawal Criteria	The following withdrawal/discontinuation criteria are defined for the study: 1. Patient develops a stage III, IV or unstageable pressure ulcer or any other deep tissue injury in the study area 2. Patient develops a fungal, bacterial or viral infection or other condition requiring the use of topical medication or product in the area treated with IAD products 3. Patient develops any condition which, in the opinion of the Investigator, requires discontinuation from the study including pregnancy
Period of Patient's Participation	21 days in maximum
Sample Size	Due to the exploratory design no formal a priori hypothesis is defined. The intention is to learn more about the effect size of certain variables such as healing outcome when compared to different local IAD care regimes in hospitals. The results of the study will be used to examine the feasibility of a potential subsequent confirmatory RCT.

	Total: n = 60 patients Stratum 1: n = 30 IAD 1A patients (persistent redness without clinical signs of infection) Stratum 2: n = 30 IAD 2A patients (skin loss without clinical signs of infection) The patients will be allocated 1:1 to either Cavilon Advanced Skin Protectant or hospital IAD standard care. Each site is expected to recruit 10 IAD 1A and 10 IAD 2A patients: 5 IAD 1A patients allocated to Cavilon Advanced Skin Protectant 5 IAD 1A patients allocated to hospital IAD care 5 IAD 2A patients allocated to Cavilon Advanced Skin Protectant 5 IAD 2A patients allocated to hospital IAD care
Randomization	Stratified randomization with regard to different IAD categories: Stratum 1: IAD 1A (50% of the patients) Stratum 2: IAD 2A (50% of the patients) The patients will be allocated 1:1 to either Cavilon Advanced Skin Protectant or hospital IAD standard care
Geography	United Kingdom, Germany, Belgium
# Sites	3 sites (1 in UK, 1 in Germany, 1 in Belgium) # patients per site: 20 patients per site (10 IAD 1A patients and 10 IAD 2A patients) Depending on the recruitment rate the sponsor reserves the right to allow for competitive recruitment or to add additional sites. Each site includes at least 10 patients.
Study Length	10 months including an enrollment period of 9 months.
Data Analysis Planned	Intention-to-treat analysis (performance/safety) Per-protocol analysis (performance) All quantitative data will be summarized with descriptive statistics.

2. Background information

Incontinence-associated dermatitis is defined as skin damage caused by exposure to urine and/or stool [1]. The clinical appearance ranges from painful erythema to severe erosion and denudation/skin loss with or without secondary infection. IAD is a type of irritative contact dermatitis triggered by increased skin surface moisture, irritants from urine and feces (e.g. digestive enzymes), increased skin temperature (e.g. due to occlusive diapers), and repeated cleansing activities. An increased load of intestinal bacteria on the skin surface in combination with skin maceration have been shown to contribute to more severe forms of IAD [2].

IAD is a common problem in healthcare settings and can be difficult to treat. Studies have estimated prevalence rates from 5.6% to 50% [3-7] and incidence rates between 3.4% – 25% [8-10] depending on the type of setting and population studied. Patients in intensive care units and elderly patients are considered to be at a particular high risk. IAD and pressure ulcers have a number of risk factors in common. Both conditions are most likely to occur in patients who have poor health and problems with mobility [11, 12, 13]. A frequent complication of patients with IAD are secondary skin infections, candidiasis being one of the most common secondary infections associated with IAD [7].

The type of incontinence and frequency of episodes (especially fecal) belong to the key risk factors for IAD. Clinicians generally agree that fecal incontinence puts the skin at higher risk for damage than exposure to urine alone [6, 14, 15]. This is due to the presence of high levels of lipid- and protein-digestive enzymes attacking the stratum corneum. The highest risk of skin damage is linked to liquid feces (diarrhea) with extraordinary high levels of digestive enzymes [16,17]. Double incontinence with combination of urine and feces can aggravate the condition. The enzymes can also act on urea and produce ammonia, further increasing the pH to the optimum of enzyme activity [18]. Poor skin condition (e.g. due to aging/steroid use/diabetes), compromised mobility, critical illness, medications (antibiotics, immunosuppressants), pain, poor nutritional status, diminished cognitive awareness and inability to perform personal hygiene are further risk factors as well as raised body temperature (pyrexia) and the use of occlusive containment products [3, 5, 16, 19, 20].

The problem of IAD receives increasing attention worldwide. Best practice principles for IAD prevention and management strategies were published in 2015 by a global expert panel [1]. Based on differential IAD diagnosis and considering the individual causes and risk factors the comprehensive care plans follow two principles: avoiding contact of urine and/or stool to the skin, and providing a structured skin care regimen. The therapy usually starts with the choice of appropriate device for fluid management. Adult briefs, absorbent pads and diapers are frequently

used for fluid management but might hold the moisture against the skin if occlusive. Therefore newer products with improved fluid handling properties should be considered as an adjunct to a structured skin care regimen. Patients in acute settings may require temporary diversion of urine and/or faces away from the skin to allow adequate skin protection and/or healing. Indwelling urinary catheter are used to avoid contact of urine to the skin but are often linked to a higher risk of nosocomial infection. While fecal management systems are used with increasing frequency to contain and divert liquid feces from the perineal skin (21, 22, 23), exposure can still occur due to device leakage. Consequently, a structured skin care regimen remains a critical consideration.

A structured skin care regime consists of two key interventions: gentle cleansing of the skin to remove urine and/or feces and protecting the skin to avoid or minimize exposure to urine and/or feces and friction. No-rinse skin cleansers with a pH similar to normal skin or pre-moistened incontinence care wipes are recommended for gentle cleansing followed by the application of skin protectants to build up a barrier between the stratum corneum and any moisture or irritant. A wide range of creams, ointments, pastes, lotions and films are available based on different skin barrier formulations such as petrolatum-based, dimethicone-based, zinc oxide-based, or liquid film-forming acrylate [24]. However, severe IAD with weeping denudement remains difficult to treat because most skin barrier products cannot stick to weepy skin and have to be applied as a thick layer on top of the wound. In some cases of severe IAD wound dressings that promote moist wound healing are used even though the application is challenged by skin contours such as folds and creases, and the presence of moisture.

In this study the effects of 3M™ Cavilon™ Advanced Skin Protectant regarding IAD management and outcome will be assessed in comparison to hospital standard care practice in Western Europe. The CE-marked medical device is designed for the use on conditions involving partial-thickness skin loss such as severe IAD and to attach to intact as well as denuded, weepy skin. The liquid is based on a new cyanoacrylate chemistry designed to polymerize *in situ*. Upon application to skin, the liquid dries rapidly to form a breathable highly durable film barrier able to protect the skin surface from external irritants such as feces [25]. It is elastomeric, adhering to contours of the skin that are difficult to dress. The product was tested in care settings of the United States and in comparison to United States IAD standard care. The study is designed as an exploratory study to find out the effect size of certain screening variables such as healing outcome when compared to the different local IAD care regimes and will consider the medical routine of Western European hospitals regarding IAD care under real-world circumstances.

2.1 Identification and description of the study device

2.1.1 Summary description of the study device

3M™ Cavilon™ Advanced Skin Protectant is a polymeric-cyanoacrylate solution intended to cover and protect 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-cyanoacrylate 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 (i.e., superficial, partial thickness skin loss) 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

3M™ Cavilon™ Advanced Skin Protectant is a CE-marked class IIa medical device according to the Medical Device Directive 93/42/EEC, Annex IX, rule 4.

2.1.2 Intended purpose and intended purpose in the clinical investigation

Cavilon Advanced Skin Protectant forms a film barrier intended to cover and protect intact or damaged skin. It is effective in conditions where wet and/or dry skin is frequently or continuously exposed to moisture and caustic irritants such as feces, digestive fluids, wound drainage and urine. The protective film barrier reduces pain associated with Incontinence-Associated Dermatitis and prevents, stops, and/or reverses the effects of IAD. 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 allowing/enabling the skin to heal.
In this study the effects of Cavilon Advanced Skin Protectant will be assessed regarding the treatment of IAD category 1A (persistent redness without clinical signs of infection) and IAD category 2A (skin loss without clinical signs of infection).

2.1.3 Population and indication study device is intended

Cavilon Advanced Skin Protectant is intended for the treatment of Incontinence-associated dermatitis and will be used within its intended use in this study. The study population is characterized by hospitalized incontinent patients with IAD category 1A (persistent redness without clinical signs of infection) or IAD category 2A (skin loss without clinical signs of infection).

2.1.4 Summary of necessary training

The study nurses will be trained with regard to accurate IAD skin assessment and product application of Cavilon Advanced Skin Protectant according to the manufacturer's instructions for use. In addition the study nurses will receive a training with regard to digital photography and all necessary study documentation.

2.1.5 Traceability and labeling

Cavilon Advanced Skin Protectant bears the CE-Mark and is labeled accordingly**.** The study supplies will be delivered in their original sales packaging to the sites. Traceability is ensured by the indication of the lot numbers.

2.1.6 Other material labeling

Not applicable

3. Justification of the design of the clinical investigation

This study is an exploratory RCT to assess the effects of Cavilon Advanced Skin Protectant in comparison to the local IAD care regimes of Western European hospitals. Due to the exploratory design no formal a priori hypothesis is defined. The intention is to learn more about the effect size of certain variables such as healing outcome when compared to different local IAD care regimes in hospitals. The results of the study will be used to examine the feasibility of a potential subsequent confirmatory RCT.

4. Risk and benefits of the study device and clinical investigation

4.1 Anticipated clinical benefits

Cavilon Advanced Skin Protectant forms a film barrier intended to cover and protect intact or damaged skin. It is effective in conditions where wet and/or dry skin is frequently or continuously exposed to moisture and caustic irritants such as feces, digestive fluids, wound drainage and urine. The protective film barrier reduces pain associated with Incontinence-Associated Dermatitis and prevents, stops, and/or reverses the effects of IAD. One intention of this study is to assess if IAD patients treated with Cavilon Advanced Skin Protectant achieve a better and/or faster healing outcome in comparison to patients treated with the local IAD care regime of the hospital.

4.2 Anticipated adverse device effects.

According to the warnings described in the manufacturer's Instructions for Use the use of Cavilon Advanced Skin Protectant on individuals who are allergic to any of the ingredients should be avoided. An anticipated adverse device effect is therefore an allergic reaction to Cavilon Advanced Skin Protectant.

4.3 Residual risks associated with the study device

The following contraindications and warnings are described in the manufacturer's Instructions for Use.

Contraindications:

Cavilon Advanced Skin Protectant is NOT to be used:

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

Warnings:

1. DANGER! HIGHLY FLAMMABLE!
2. Cavilon Advanced Skin Protectant is highly flammable until it has completely dried on the skin.
3. The product should only be applied when no ignition sources or heat-producing devices are in use.
4. Avoid using the product around flames.

5. Use the product only in well ventilated areas.
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. The product 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.

4.4 Risks associated with participation in the clinical investigation.

The potential risks associated with participation in the clinical study are considered to be similar with those risks associated with other IAD skin protectant products used for the treatment of IAD in the hospital routine. According to the manufacturer's Instructions for Use one potential risk could be an allergic reaction to any of the ingredients of Cavilon Advanced Skin Protectant. The liquid of Cavilon Advanced Skin Protectant is highly flammable and care should be taken not to apply the product in the presence of heat-emitting devices or open flames (e.g. candle) until the barrier film has dried.

4.5 Possible interactions with concomitant medical treatments.

The following precautions with regard to concomitant medical treatments are described in the manufacturer's Instruction for Use:

<u>Precautions:</u>

- 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.
- Use of other barrier products, ointments, creams or lotions may significantly reduce the effectiveness of the product.
- The product can increase the adhesion of some adhesive products (e.g. tape), particularly in the first few days of use. When removing an adhesive product, it is important to exercise care and follow the Instructions for Use.

4.6 Steps that will be taken to control or mitigate the risks.

The following steps will be taken to control or mitigate the risks:

- All investigators are selected with regard to their profound expertise regarding IAD management.
- Research study nurses will be trained on the manufacturer's Instruction for Use.
- Specific inclusion/exclusion criteria are defined to enroll appropriate patients
- The skin of the patients will be assessed daily during the study

Risks are minimized at the clinical site through:

- Compliance with the manufacturer's Instruction for Use
- Compliance with this study protocol
- Close monitoring of the patient's status during study participation

4.7 Risk-to-benefit rationale

Cavilon Advanced Skin Protectant was tested in an open label, non-randomized prospective study in the United States (ClinicalTrials.gov. Identifier: NCT02724449; publication free text available [32]). The purpose of the study was to evaluate the efficacy of Cavilon Advanced Skin Protectant at managing severe skin breakdown associated with incontinence. The sample comprised 16 patients; inclusion criteria were: patients older than 18 years, cared for in the intensive care unit of a level I trauma center hospital or in long-term care facilities in the northeast region of the United States, and had incontinence-associated dermatitis (IAD). Twelve of the patients had epidermal skin loss and 4 had severe redness. The IAD score improved in 13 of 16 patients, remained unchanged in 1 patient, and deteriorated in 2 patients. The median percent improvement in the skin assessment instrument was 96% ($p = .013$). Four of the patients with epidermal skin loss had complete reepithelialization of the skin surface with 4 to 6 applications of the skin protectant, and 5 had substantial improvement. The 4 patients with severe red skin returned to healthy normal skin with 2 to 4 skin protectant applications. Substantial pain reduction was reported by all 9 patients who reported pain at enrollment. No adverse events associated with the skin protectant application were reported during data collection.
The product is currently tested against zinc oxide paste in a randomized controlled trial in the United States (ClinicalTrials.gov Identifier: NCT02570139).

Based on the reported clinical data it is concluded that the product meets the claims according to the manufacturer's Instructions for Use, and that potential undesirable clinical effects and risks can be controlled and are acceptable, when weighed against the benefits of IAD therapy.

5. Objectives and hypotheses of the clinical investigation

5.1 Objectives

The objective of the study is to assess the effects of 3M Cavilon Advanced Skin Protectant in comparison to the local IAD care regimes of Western European hospitals. Due to the exploratory design of the study the objectives are not divided into primary and secondary objectives. The study is designed as an exploratory study to learn more about the effect size of certain variables such as healing outcome when compared to different local IAD care regimes and will consider the medical routine of Western European hospitals regarding IAD care under real-world circumstances. Due to the exploratory design no formal a priori hypothesis is defined. The results of the study will be used to examine the feasibility of a potential subsequent confirmatory RCT.

5.2 Hypothesis

The study is of exploratory design and no formal a priori hypothesis is defined.

5.3 Claims and intended performance

The claims and intended performance described in the manufacturer's Instructions for Use were supported with laboratory and clinical data generated in the United States. This study will test the product performance under the medical routine of European hospitals. The performance will be compared to local IAD management regimes.

5.4 Anticipated risks and adverse device effects

According to the warnings described in the manufacturer's Instructions for Use an allergic reaction to Cavilon Advanced Skin Protectant would constitute an anticipated adverse event in this study.

6. Statistical consideration

6.1 Statistical design, method and analytical procedures

This study is designed as an exploratory RCT to measure possible effects of Cavilon Advanced Skin Protectant in the management of IAD when compared to local IAD care regimes (please refer to the study endpoints for more details). The treatment will be integrated into the daily medical routine of the hospitals to assess the effects in comparison to the local IAD care under real-world circumstances.

All quantitative data such as demographics, IAD history, IAD skin assessments, pain assessments will be summarized with descriptive statistics. In general continuous variables will be summarized using the following standard descriptive summary statistics: number of observations, arithmetic mean, standard deviation, minimum, median, maximum. Categorical variables will be displayed by means of frequency tables and, where appropriate, shift tables.

The statistical analyses will be based on analysis sets defined as follows:

Full analysis set including safety:

The full/safety analysis set will include all patients enrolled

Per-protocol analysis set:

The per-protocol analysis set – being a subset of the full analysis set – will only include patients who complete treatment of at least five days. Additionally, patients with major protocol violations which may have an impact on efficacy evaluation will be excluded from the per-protocol analysis set.

The determination of major protocol violations which may have an impact on the statistical analyses and the resulting definition of analysis sets will be performed prior to start of any statistical analyses. A summary of the number of patients per analysis set will be given and reasons for exclusion of a patient from an analysis set will be listed.

The statistical analysis will be performed using the software package SAS® version 9.3 or higher (SAS Institute Inc., Cary, NC 27513, USA).

6.2 Sample size

Due to the exploratory design no formal a priori hypothesis is defined. The intention is to learn more about the effect size of certain variables such as healing outcome when

compared to different local IAD care regimes in hospitals. The results of the study will be used to examine the feasibility of a potential subsequent confirmatory RCT.

Total: n = 60 patients

Stratum 1: n = 30 IAD 1A patients
(persistent redness without clinical signs of infection)

Stratum 2: n = 30 IAD 2A patients
(skin loss without clinical signs of infection)

The patients will be allocated 1:1 to either Cavilon Advanced Skin Protectant or hospital IAD standard care regime.

Each site is expected to recruit 10 IAD 1A and 10 IAD 2A patients for the study:

5 IAD 1A patients allocated to Cavilon Advanced Skin Protectant

5 IAD 1A patients allocated to hospital IAD care

5 IAD 2A patients allocated to Cavilon Advanced Skin Protectant

5 IAD 2A patients allocated to hospital IAD care

6.3 Level of significance and power

Not applicable

6.4 Expected drop-out rate

The sample size of 60 patients includes an anticipated drop-out rate of 20%.

6.5 Pass/Fail criteria

Not applicable

6.6 Provision for interim analysis (if applicable)

Not applicable

6.7 Termination criteria

Termination criteria for the study are described under chapter 19.

6.8 Deviations

A statistical analysis plan will be prepared for the study. The statistical analysis plan will becompleted before data lock. Any deviation(s) from the statistical analysis plan will be described and justified in the final report.

6.9 Subgroup specification

Subgroups are specified with regard to different IAD severity categories.
IAD category 1A: persistent redness without clinical signs of infection
IAD category 2A: skin loss without clinical signs of infection

6.10 Procedures that take into account all the data

All data will be presented in individual patient data listings.

6.11 Procedures for accounting missing, unused or spurious data

Missing critical data about effects such as first time observation for 100% re-epithelialization of skin loss and complete healing of IAD without any signs of erythema will be imputed. Patients excluded from any subset or per protocol analysis will be documented and justified.

6.12 Patient calculation per center

Each center is expected to recruit 20 eligible patients for the study (n = 10 IAD 1A patients; n = 10 IAD 2A patients). Depending on the recruitment rate the sponsor reserves the right to allow for competitive recruitment or to add additional centers. Each center includes at least 10 patients.

7. Design of the clinical investigation

7.1 Clinical investigational type

This is a multi-centre, multi-country, prospective, randomized controlled trial.
CE-marked study device will be used within the intended use according to the manufacturer's Instructions for Use.

7.2 Randomization and blinding

The random numbers will be generated by computer. The randomization is stratified with respect to two different IAD severity categories according to the Ghent Global IAD Categorization Tool [33; appendix 24.2]. Stratum 1 is defined as IAD category 1A (persistent redness without clinical signs of infection) and Stratum 2 as IAD category 2A (skin loss without clinical signs of infection). The strata are of same sizes (50:50 ratio). The participants will receive either Cavilon Advanced Skin Protectant or the local hospital IAD care products within the same stratum. Due to the obvious differences between the comparative hospital IAD care prodcuts and the study device, the study nurses cannot be blinded. A blinded assessor will assess the healing outcome based on the photographs of the study area that is defined as the sacral region going down to the upper thighs, bordered approximately 5 cm below the gluteal fold.

7.3 Endpoints

Due to the exploratory design of the study the endpoints are not divided into primary and secondary endpoints.
The following endpoints are defined for the study with regards to the comparison of Cavilon Advanced Skin Protectant and local IAD hospital care:

1. Number and percentage of patients completely healed
   (skin free of any IAD signs, including erythema)
2. Number and percentage of patients improved with regard to IAD category
3. Number and percentage of patients with 100% re-epithelialization of skin loss
   (skin loss: skin is moist, as the epidermal layer is missing)
4. Time to complete healing or reduction in IAD category
5. Protection of IAD category 1 patients from developing IAD category 2
6. Prevention with regard to IAD recurrence
7. Material cost based on product utilization such as type of products, frequency of application and days of treatment
8. Use of resources involved in the IAD therapy
9. Nursing time to clean up incontinence and to administer IAD treatment products
10. Pain scores with regard to cleansing procedure and application of IAD product
    (Wong-Baker FACES® Pain Rating Scale: assessment only for cognitively healthy patients according to the judgement of the study nurse)

11. Number and percentage of patients with adverse events and the nature of each adverse event

7.4 Methods and timing for assessing, recording and analysing variables

Appendix 24.1 presents the study schedule with timing (Flowchart). The assessment methods with instructions are described in detail under chapter 11.
Informed consent shall be obtained in writing from the patient or patient's legally authorized representative and the process shall be documented before any procedure specific to the study is applied to the patient. Informed consent may be given by the legally authorized representative only if a patient is unable to make the decision to participate in the study (e.g. seriously ill or unconscious patient, mentally ill person, mentally handicapped person). In such cases, the patient shall also be informed about the study within his/her ability to understand.

Study Schedule: Day 01

1. Review the inclusion and exclusion criteria
2. Randomize the patient to the allocation group (3M study device or hospital IAD standard care)
3. Complete patient demographics (gender, age, height, weight, main reason for hospitalization)
4. Record IAD history (date of IAD diagnosis if known, IAD status, IAD occurrence first/recurrent, incontinence type, comorbidities)
5. Obtain current concomitant medication
6. Capture information with regard to the Barthel Index
7. Complete the Braden Scale for Predicting Pressure Sore Risk
8. Perform skin cleansing
9. Ask the patient to indicate the IAD pain level before and during cleansing using the Wong-Baker FACES® Pain Rating Scale (assessment only for cognitively healthy patients according to the judgement of the study nurse)
10. Perform a structured IAD skin assessment according to the GLOBIAD Tool. Estimate the IAD affected area in cm^2 using the measurement sheet provided by the sponsor (either of the total affected IAD area inclusive signs of erythema or with focus on skin loss only). Fill out the IAD study diary with regard to skin assessment information.

11. Take photographs of the study area according to the site procedure manual. Upload the photographs into the photo database.
12. Depending on the randomization allocation apply Cavilon Advanced Skin Protectant or the IAD hospital standard care product
13. Ask the patient to indicate the IAD pain level before, during and after the application of Cavilon Advanced Skin Protectant or the IAD hospital standard care product using the Wong-Baker FACES® Pain Rating Scale (assessment only for cognitively healthy patients according to the judgement of the study nurse). Document observations regarding weeping/exuding and bleeding after product application.
14. Track IAD care information over the day/night and fill out the IAD study diary (incontinence status, use of urinary catheter, use of fecal management system, frequency of absorbent pad or diaper changes, frequency of intimate cleansing procedures, application frequency of IAD care products, IAD specialist appointments/visits)
15. Capture detailed information with regard to the use of certain IAD care products in the study such as cleansing products, skin protectants building up the moisture barrier, IAD wound dressings or other products if applicable [product name, treatment duration period, product type, manufacturer, REF number (indicates the manufacturer's catalogue number so that the medical device can be identified), packaging unit, number of containments used for the study]
16. Record adverse events, if applicable
17. Record protocol deviations, if applicable

Study Schedule: Day 02 – Day 20

1. Perform skin cleansing
2. Day 04, Day 07, Day 10, Day 13, Day 16, Day 19, End of Study (discontinuation): Ask the patient to indicate the IAD pain level before and during cleansing using the Wong-Baker FACES® Pain Rating Scale (assessment only for cognitively healthy patients according to the judgement of the study nurse).
3. Day 04 IAD Nursing Time**:** Measure the time taken to clean up incontinence (front/back) and the time taken to administer the IAD treatment products to the study area that is defined as the sacral region going down to the upper thighs, bordered approximately 5 cm below the gluteal fold (patients assigned to Cavilon Advanced Skin Protectant and patients assigned to the local hospital IAD care regime). Please consider the nursing time measurement instructions (stopwatch and scale provided by the sponsor). Measure the

weight of the skin protectant building up the moisture barrier before and after application if the patient is assigned to the local hospital IAD care regime group.

4. Perform a structured IAD skin assessment according to the GLOBIAD Tool. Estimate the IAD affected area in cm^2 using the measurement sheet provided by the sponsor (either of the total affected IAD area inclusive signs of erythema or with focus on skin loss only). Fill out the IAD study diary with regard to skin assessment information.
5. Photographs should be taken on Day 04, 07, 10, 13, 16, 19 and End of Study (Day 21 or discontinuation). Additional photos should also be taken at the first day no evidence of IAD is present (e.g. no erythema, no skin damage), i.e. transition from IAD1 to IAD free. If a patient has IAD 2 skin lesions/skin loss, additional photos should be taken on the first day of 100% re-epithelialization, i.e. IAD2 transition to IAD 1. Photographs must be taken according to the site procedure manual. Photos must be uploaded into the database if they refer to a study endpoint – either Day 01, Day 21, IAD2 to IAD1 or IAD1 to IAD free. Photos should be kept on the respective SD memory cards, labelled according to the site procedure manual and stored in the IAD study diary.
6. Depending on the randomization allocation apply Cavilon Advanced Skin Protectant (Day 04, Day 07, Day 10, Day 13, Day 16, Day 19) or the IAD hospital standard care product following the hospital medical routine/interval
7. Day 04, Day 07, Day 10, Day 13, Day 16, Day 19 (+/- 1 day):
   Ask the patient to indicate the IAD pain level before, during and after the application of Cavilon Advanced Skin Protectant or the IAD hospital standard care product using the Wong-Baker FACES® Pain Rating Scale (assessment only for cognitively healthy patients according to the judgement of the study nurse). Document observations regarding weeping/exuding and bleeding after product application.
8. Track IAD care information over the day/night and fill out the IAD study diary (incontinence status, use of urinary catheter, use of fecal management system, frequency of absorbent pad or diaper changes, frequency of intimate cleansing procedures, application frequency of IAD care products, IAD specialist appointments/visits)
9. Capture detailed information with regard to the use of certain IAD care products such as cleansing products, skin protectants building up the moisture barrier, IAD wound dressings or other products if applicable [product name, treatment duration period, product type, manufacturer, REF number (indicates the manufacturer's catalogue number so that the medical device can be identified), packaging unit, number of containments used for the study]

10. Record adverse events if applicable
11. Record protocol deviations if applicable

NOTE: Any recurrence of IAD in both study groups is to be examined. If the hospital routinely does not use IAD prevention products, the recurrence of IAD is still to be observed for the group allocated to hospital IAD standard care. In this case, the study procedures of “Application: Comparator” and “Pain Score: Application” no longer apply (Appendix 24.1 B).

Study Schedule: End of Study (Day 21 or discontinuation)

1. Perform skin cleansing
2. Ask the patient to indicate the IAD pain level before and during cleansing using the Wong-Baker FACES® Pain Rating Scale (assessment only for cognitively healthy patients according to the judgement of the study nurse).
3. Perform a structured IAD skin assessment according to the GLOBIAD Tool. Estimate the IAD affected area in cm^2 using the measurement sheet provided by the sponsor (either of the total affected IAD area inclusive signs of erythema or with focus on skin loss only). Fill out the IAD study diary with regard to the skin assessment information.
4. Take photographs of the study area according to the site procedure manual. Upload the end of study photos into the photo database.
5. Track IAD care information and fill out the IAD study diary (incontinence status, use of urinary catheter, use of fecal management system, frequency of absorbent pad or diaper changes, frequency of intimate cleansing procedures, IAD specialist appointments/visits). Collect the IAD study diary at the end of the study.
6. Check the completeness of the information with regard to the use of certain IAD care products at the end of the study
7. Record adverse events if applicable
8. Record protocol deviations if applicable

7.5 Equipment

The following equipment will be provided by the sponsor to the sites:

Digital photography equipment

IAD Measurement Sheet

Stopwatch

Scale

7.6 Replacement of patients

Patients who discontinue before the first product application will be replaced with another patient.

8. Study device(s) and comparator(s)

8.1 Description of the exposure

Cavilon Advanced Skin Protectant will be applied every 72 hours in this study.
The comparator products will be applied according to the local hospital IAD care intervals following the hospital medical routine.

8.2 Number of study devices

Cavilon Advanced Skin Protectant will be applied 7 times in maximum for a study period of 21 days. Sufficient amounts of applicators will be shipped to the study centers.

8.3 Justification of the choice of comparator(s)

The intention of the study is to assess the effects of Cavilon Advanced Skin Protectant in comparison to local hospital IAD standard care regime. In the comparator group the patients will be treated with the usual hospital IAD care products according to the medical routine of the hospital.

8.4 Other medical device or medication

Not applicable

8.5 Regulatory requirements of study material

3M™ Cavilon™ Advanced Skin Protectant is a CE-marked medical device class IIa according to the Medical Device Directive 93/42/EEC, Annex IX, rule 4.

9. Patients

9.1 Inclusion criteria

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

1. Is the patient 18 years or older?
2. Has the patient or their legally authorized representative signed the Informed Consent Form?
3. Does the patient have IAD category 1A or IAD category 2A in the study area*?
4. Is the patient incontinent and does stool and/or urine come into direct contact with the skin?
5. Is the patient able to be turned/positioned with regard to skin assessment and photo documentation?
6. Is there a reasonable expectation that the patient will remain in the hospital setting for at least 7 days?

*NOTE: Study Area
The study area is defined as the sacral region going down to the upper thighs, bordered approximately 5 cm below the gluteal fold.


Study Area: IAD has to be present in this zone at the start of the study

9.2 Exclusion criteria

Patients are excluded from participation in this study if any of the answers to these questions are yes.

1. Is the patient pregnant or breast feeding?
2. Does the patient have a known hypersensitivity or allergy to acrylate or cyanoacrylate?
3. Does the patient have a stage II, III, IV or unstageable pressure ulcer or other suspected deep tissue injury in the study area?
4. Does the patient require topical treatment due to a fungal, bacterial or viral infection in the study area?
5. Does the patient require treatment with topical medication or product other than IAD treatment in the study area?

6. Does the patient have any other local dermatological disease or skin condition interfering with this study?
7. Does the patient have any medical condition (e.g. end of life, planned elective surgery) that in the opinion of the investigator should exclude him/her from participating in the study?
8. Does the patient participate in another study with a known or implied effect on skin barrier function?

9.3 Criteria and procedures for patient withdrawal or discontinuation

The following withdrawal/discontinuation criteria are defined for the study:

1. Patient develops a stage III, IV or unstageable pressure ulcer or any other deep tissue injury in the study area.
2. Patient develops a fungal, bacterial or viral infection or other condition requiring the use of topical medication or product in the area treated with IAD products.
3. Patient develops any condition which, in the opinion of the Investigator, requires discontinuation from the study including pregnancy.

   The date and reason for withdrawal/discontinuation will be documented in the “end of study” documentation and recorded as adverse event if applicable.

9.4 Point of enrolment

The patient is enrolled for the study if the patient meets all inclusion and exclusion criteria and signed the informed consent form.

9.5 Total expected duration

The total expected duration of the study is 10 months including an enrollment period of 9 months.

9.6 Expected duration of each patient’s participation

The maximum duration of each patient’s participation is 21 days. If IAD heals before 21 days and the patient is still incontinent, the patient will stay in the study to assess IAD recurrence rate with continued application of the study device (Cavilon Advanced Skin Protectant) or in the case the patient is allocated to the local IAD care regime with products following the local

IAD prevention regime. If IAD heals before 21 days and incontinence discontinued or incontinence constituents are not in direct contact with the skin anymore, the patient will be released from the study. Patients discharged from the hospital prior to 21 days fulfill the requirements for study completion and are not followed-up outside of the hospital.

The maximum patient participation is 21 days. If IAD heals before 21 days and the patient is still incontinent, the patient will stay in the study in order to assess the IAD recurrence rate. The patient will continue treatment either with Cavilon Advanced Skin Protectant or the local IAD care regime depending on the assigned study arm.

If IAD heals before 21 days and the patient is no longer incontinent (or incontinence constituents are not in direct contact with the skin anymore) the patient will be released from the study irrespective of allocation group.

Patients that have completed at least 5 days, but terminate the study prior to 21 days i.e. due to hospital discharge, fulfill the requirements for study completion and are not followed-up outside of the hospital.

Note: Any recurrence of IAD in both study groups is to be examined. If the hospital routinely does not use IAD prevention products, the recurrence of IAD is still to be observed for the group allocated to standard care. In this case, the study procedures of “Application: Comparator” and “Pain Score: Application” no longer apply (Appendix 24.1 B).

9.7 Number of patients required

Due to the exploratory design no formal a priori hypothesis is defined. The intention is to learn more about the effect size of certain variables such as healing outcome when compared to different local IAD care regimes in hospitals. The results of the study will be used to examine the feasibility of a potential subsequent confirmatory RCT.

Total: n = 60 patients

Stratum 1: n = 30 IAD 1A patients
(persistent redness without clinical signs of infection)

Stratum 2: n = 30 IAD 2A patients
(skin loss without clinical signs of infection)

The patients will be allocated 1:1 to either Cavilon Advanced Skin Protectant or hospital IAD standard care.

Each site is expected to recruit 10 IAD 1A and 10 IAD 2A patients:

5 IAD 1A patients allocated to Cavilon Advanced Skin Protectant

5 IAD 1A patients allocated to hospital IAD care

5 IAD 2A patients allocated to Cavilon Advanced Skin Protectant

5 IAD 2A patients allocated to hospital IAD care

9.8 Enrolment period

The enrollment period is expected to be 9 months.

10. Treatment of patients

The patients will be treated either with Cavilon Advanced Skin Protectant (study device) or IAD hospital standard care (comparator)

Treatment with Cavilon Advanced Skin Protectant

Cavilon Advanced Skin Protectant will be applied to the study area that is defined as the sacral region going down to the upper thighs, bordered approximately 5 cm below the gluteal fold (IAD affected as well as unaffected skin). The genital area and the frontal skin folds will be treated only in case of visible IAD and only for the IAD affected skin. In consideration of the manufacturer's instruction for use no topical medication or other product shall be applied on top of the barrier film because the effectiveness of either film or medication might be reduced.

Application Cavilon Advanced Skin Protectant

 Complete Area (Treatment/Prevention)  ONLY VISIBLE IAD (Treatment)

Treatment with IAD hospital standard care products

The hospital standard care products of the comparator group will be applied to the skin areas following the local hospital procedures and considering the manufacturers' instructions for use especially with regard to contraindications. The use of topical medication or product other than the IAD treatment is not allowed for the study area in the comparator group.

11. Assessment of effects/performance

11.1 Effect/performance parameters

Cavilon Advanced Skin Protectant in comparison to IAD Hospital Standard Care

IAD Healing/Improvement

- ✓ IAD severity category according to the Ghent Global IAD Categorization Tool [33] evaluated by the research study nurses on-site
  IAD 1A: persistent redness without clinical signs of infection
  IAD 1B: persistent redness with clinical signs of infection
  IAD 2A: skin loss without clinical signs of infection
  IAD 2B: skin loss with clinical signs of infection
  IAD free: skin free of any IAD signs, including erythema
- ✓ IAD affected area in cm^2 evaluated by the research study nurses on-site
  Total IAD affected area inclusive signs of erythema (measurement sheet estimate)
  Area affected by IAD skin loss (measurement sheet estimate)
- ✓ IAD severity category according to the GLOBIAD Tool evaluated by the blinded assessor based on the photographs of the study area that is defined as the sacral region going down to the upper thighs, bordered approximately 5 cm below the gluteal fold.
  IAD 1A: persistent redness without clinical signs of infection
  IAD 1B: persistent redness with clinical signs of infection
  IAD 2A: skin loss without clinical signs of infection
  IAD 2B: skin loss with clinical signs of infection
  IAD free: skin free of any IAD signs, including erythema
- ✓ IAD affected area in cm^2 traced by the blinded assessor based on the photographs of the study area.
  Total IAD affected area inclusive signs of erythema (software calculation in cm^2)
  Area affected by IAD skin loss (software calculation in cm^2)
- ✓ Time to healing in days
  Number of days to achieve improvement in severity category according to the GLOBIAD Tool or days until complete healing without any signs of erythema

Prevention of IAD Deterioration and Recurrence

- ✓ IAD severity category according to the Ghent Global IAD Categorization Tool evaluated by the research study nurses on-site and the blinded assessor based on the photographs of the study area.

Pain Assessment

(only for cognitively healthy patients according to the judgement of the study nurse

- ✓ IAD pain scores according to the Wong-Baker FACES® Pain Rating Scale at the start and the end of the study (pain scores 0 – 10)
- ✓ Pain scores according to the Wong-Baker FACES® Pain Rating Scale associated with the incontinence cleanup (pain scores 0 – 10)
- ✓ Pain scores according to the Wong-Baker FACES® Pain Rating Scale associated with the IAD product application (pain scores 0 – 10)

Material cost and resource use

- ✓ Material cost based on the information with regard to the utilization of certain IAD care products such as cleansing products, skin protectants building up the moisture barrier, IAD wound dressings or other products, their used quantity, application frequency and duration of use.
- ✓ Resources involved in the IAD therapy (e.g. number of nurses or specialists/ number of interventions)

IAD Nursing Time

- ✓ Time taken to clean up incontinence in minutes
- ✓ Time taken to apply the skin protectant building up the moisture barrier and other products that might be needed to prepare the skin (e.g. lotions to dry-out lesions before applying the skin protectant building up the moisture barrier)

11.2 Assessment method

Barthel Index [26]

The Barthel Index will be completed at the start of the study to characterize the patients with regard to their degree of independence in activities of daily living. The evaluation addresses 10 items: help needed with feeding, help needed with transfers e.g. from chair to bed, help needed with grooming, help needed with toilet use, help needed with bathing, help needed

with walking, help needed with climbing stairs, help needed with dressing, presence or absence of fecal incontinence and presence or absence of urinary incontinence. The possible scores range from 0 – 100, with lower score indicating increased disability.

Braden Scale for Predicting Pressure Sore Risk [29, 30]

The Braden Scale will be completed at the start of the study to assess the patient's level of risk for development of pressure ulcers. The evaluation is based on six indicators: sensory perception, moisture, activity, mobility, nutrition, and friction or shear. Total possible scores range from 6-23, with lower score indicating a higher risk of developing a pressure ulcer.

Wong-Baker FACES® Pain Rating Scale [31]

This pain assessment tool was originally created with children for children to help them communicate about their pain. Faces with different expressions from smiling to crying facilitate the communication as anchor for pain intensity scale 0 – 10, with higher score indicating more pain. The nurses will ask the patients to choose the face that best depicts the pain they are experiencing. Only cognitively healthy patients according to the judgement of the study nurse will be asked. The IAD pain scores will be assessed before and during cleansing following the local hospital cleansing procedure. In addition the IAD pain scores will be measured before, during and after application of the skin protectant building up the moisture barrier.

Pain assessment instructions (not valid for patients with reduced consciousness or dementia)

1. Explain to the patient that each face represents a person who has no pain (hurt), or some, or a lot of pain

Figure 1: © 1983 Wong-Baker FACES Foundation. www.WongBakerFACES.org. Used with permission

2. Face 0 doesn't hurt at all. Face 2 hurts just a little bit. Face 4 hurts a little bit more. Face 6 hurts even more. Face 8 hurts a whole lot. Face 10 hurts as much as you can imagine, although you don't have to be crying to have this worst pain.
3. Ask the patient to choose the face that best depicts the pain they are experiencing.

IAD Nursing Time

The time taken to clean up incontinence and to administer the IAD treatment products will be measured with a stopwatch at Day 04 (+/- 1 day) preferably in the presence of fecal constituents. Additionally, the skin protectant building up the moisture barrier will be weighed before and after application for those patients allocated to the usual IAD hospital care regime

Nursing Time Instructions:

Preparation:

1. Collect supplies and prepare the room
2. Familiarize with the sponsor provided stopwatch
3. Remove diapers/pads. Dispose coarse dirt that can be grabbed with a wipe.

Time to clean up incontinence (back side & front):

1. Timekeeper starts stopwatch when nurse indicates start of cleansing procedure with picking up the cleanser
2. Timekeeper stops stopwatch when nurse indicates cleansing procedure is complete (exclusive time to cleanup location)

Time to administer IAD treatment products:

Study area: Sacral region going down to the upper thighs, bordered approximately 5 cm below the gluteal fold.

1. Familiarize with the sponsor provided scale
2. Weigh the skin protectant building up the moisture barrier if the patient is allocated to the IAD hospital standard care group (content in gram before application)
3. Timekeeper starts stopwatch when nurse indicates start of application of IAD product(s) with product in hand (IAD product(s): skin protectant building up the moisture barrier and other products such as dry-out lotions to prepare the skin if needed)

4. Timekeeper stops stopwatch when nurse indicates product application is finished
5. Weigh the skin protectant building up the moisture barrier if the patient is allocated to the IAD hospital standard care group (content in gram after application)

IAD Skin Assessment

Ghent Global IAD Categorization Tool [33]

The study nurses will conduct daily skin assessments to determine the IAD severity category according to the GLOBIAD Tool definitions (appendix 24.2):

IAD 1A: persistent redness without clinical signs of infection

IAD 1B: persistent redness with clinical signs of infection

IAD 2A: skin loss without clinical signs of infection

IAD 2B: skin loss with clinical signs of infection

IAD free: skin free of any IAD signs, including erythema

The IAD severity category is to be documented in the IAD study diary.

The study nurses will receive a training regarding the GLOBIAD Tool at start of study.

In addition, the nurses will be trained in signs of infection and how to discriminate Incontinence-associated dermatitis from pressure ulcers.

Measurement Sheet to estimate the IAD affected area

The measurement sheet provided by the sponsor will be used on a daily basis to estimate the total area affected by IAD inclusive signs of erythema and in addition the area that is affected by skin loss only (skin is moist, as the epidermal layer is missing). The predefined markings of the measurement sheet will help to provide a rough estimate and to determine the cm^2 cluster range for the study documentation. All areas with IAD signs inclusive erythema or of skin loss will be summed up for the front and back side separately. The measurement sheet is to be used without contact to patient's skin.

Blinded IAD skin assessment based on photographs

All study nurses will receive an intensive training in digital photography to ensure consistent picture quality throughout the study. The nurses will take the pictures according to the instructions of the site procedure manual. The central reader will conduct a blinded skin assessment according to the independent review manual and evaluate up to four photo documentation time points per patient depending on his/her IAD severity category beginning of the study. The following photo documentation will be assessed by the central reader

according to the independent review manual:

(1) Photos at the start of the study (Day 01)

(2) Photos to confirm the endpoint of 100% re-epithelialization of IAD 2 lesions for patients that started with skin loss beginning of the study (first time)

(3) Photos to confirm the complete healing endpoint (first time; skin free of any IAD signs, including erythema)

(4) Photos at the end of the study (Day 21 or discontinuation)

The photos for the above mentioned study relevant time points will be uploaded into a photo database that enables centralized independent blinded assessor review.

All other photos taken on Day 04, 07, 10, 13, 16, 19 will be used as back-up photos for the study. The back-up photos are to be kept on the SD memory cards and stored in the IAD Study Diary. The blinded skin assessor will categorize the severity of IAD according to the GLOBIAD Tool. In addition, the blinded skin assessor will trace the area affected by IAD inclusive signs of erythema and the area affected by skin loss only. The software will calculate the area in cm^2 based on the tracing information. At the start of the study the blinded skin assessor will receive a training with regard to the tracing procedure, photography database and software.

IAD Care Assessment

The study nurses together with the ward nurses will collect the information needed to calculate the material cost based on product utilization, application frequency and days of treatment in the IAD study diary. On a daily basis the nurses will track the following information for each day stayed in the hospital during the study participation (day & night): incontinence status continued/discontinued, presence of urinary catheter or fecal management system, number of absorbent pad or diaper changes, number of intimate cleansing procedures, number of applications regarding Cavilon Advanced Skin Protectant or local IAD care products and number of IAD related visits of specialists. In addition, the IAD care products will be specified in more detail in the eCRF providing information such as product name, treatment duration period, product type, manufacturer, REF number (indicates the manufacturer's catalogue number so that the medical device can be identified), packaging unit, number of containments used for the study. The study nurses will receive a training how to document the information at the start of the study.

12. Monitoring

The present study is an international study with study sites in different European countries. Sites will be initiated in a site initiation visit. On-site monitoring visits will be conducted by sponsor or CRO authorized personnel as frequently as necessary. Monitors will record dates of the visits in a study site visit log that will be kept at the study site.

During monitoring visits, monitors will compare the data entered into the eCRFs with source documents such as the hospital or clinic records and the IAD study diary. The nature and location of all source documents will be identified to ensure that all sources of original data required to complete the eCRF are known to the sponsor and study-site personnel and are accessible for verification by the sponsor study-site contact. If electronic records are maintained at the study site, the method of verification will be discussed with the study-site personnel.

No audits are planned for the present study. The sponsor reserves the right to carry out audits if deemed necessary. Sites will be informed about the audit no less than 2 weeks prior to the audit.

The institutions (sites), the investigators and the participating patients have to agree to give monitors, auditors and inspectors (authorized persons) free access to the medical records of the study participants.

12.1 Source data

100% source data verification will be performed for patients' informed consent and key patient data. Details will be described in the Monitoring Manual. Throughout the study, sites will be monitored for patient enrolment.

Key monitoring activities at sites will comprise:

- Review and check of Investigator Site File for completeness and correctness (including positive ethics committee vote, list of EC participants, signature/delegation log, patient enrolment log, site staff qualification documentation)
- Check of signed and dated Informed Consent Form for every patient
- Check of eligibility of every patient
- Source data verification as specified in the Monitoring Manual
- Check of documentation of (S)AEs

Investigators agree to enable direct access to source documentation (medical records, IAD study diary) for the purpose of verifying data recorded in the eCRF for consistency with original source data. Findings from monitoring reviews of eCRFs and source documents will be discussed with the study-site personnel. The sponsor expects that, during monitoring visits, the relevant study-site personnel will be available, the source documentation will be

accessible, and a suitable environment will be provided for review of study-related documents.

13. Data management

13.1 Data review, database cleaning, data query management

Electronic Data Capture (eDC) will be used for this study. The study data will be transcribed by study-site personnel from the source documents into an electronic CRF, and transmitted in a secure manner to the sponsor/authorized CRO within the time agreed upon between the sponsor and the study site. The investigator's study file contains the source data location list. The investigator has to ensure accuracy, completeness and timeliness of the data reported in the eCRFs, in all required reports and in the investigator's study file. The investigator has to verify that all data entries in the eCRFs are accurate and correct.
Reportable events will be communicated to authorities and sites according to the sponsor's SOPs.
Data will be entered into a validated electronic CRF using the authorized CRO's certified electronic data capture (eDC) system. Programmed data cleaning checks will be used in addition to manual review to check for discrepancies and to ensure consistency of data. An electronic audit trail system will be maintained within the system to track all changes in the database once the data have been saved into the system. Regular backups of the electronic data will be performed. Furthermore, the CRO authorized personnel will regularly review eCRFs for accuracy and completeness during on-site monitoring visits and after transmission to the sponsor. Discrepancies will be resolved with the investigator or designee, as appropriate.
All site-related eCRF entries, corrections, and alterations must be made by the investigator or other authorized study-site personnel. If necessary, queries will be generated in the eDC tool. If corrections to data are needed after the initial entry in the eCRF, this can be done in either of the following ways:

- Investigator and study-site personnel can make corrections in the eDC tool at their own initiative or as a response to an auto query generated by the eDC tool.
- Sponsor or sponsor delegate can generate queries for resolution by the investigator and site personnel.

Any change or correction to the eCRF after first entry and saving must be accompanied by a reason for the change. Corrections made after the investigator's review and signing (by

means of a password/electronic signature) of the completed eCRF will have to be reapproved by the investigator. The investigator will have to maintain a list of personnel authorized to enter data into the eCRF.

13.2 Verification, validation and securing of eDC system

The certified eDC system used for the study database integrates numerous functions from the areas of electronic data capture, double-data-entry and data management in one application with centralized data storage. The system complies with all relevant GCP and FDA regulations, in particular with 21 CFR Part 11 offering a full audit trail, user and role management with electronic signatures. Data storage is secure and data are accessible to authorized personnel, only.

13.3 Data retention and archiving

In compliance with ICH/GCP guidelines, the investigator/ institution will maintain all eCRFs and all source documents that support the data collected from each patient, as well as all study documents, Essential Documents for the Conduct of a Clinical Trial, and all study documents as specified by the applicable regulatory requirement(s). The investigator/institution will take measures to prevent accidental or premature destruction of these documents.

Study documents and materials have to be archived at investigator sites and at the sponsor's archive for no less than 10 years. Documents will be retained for a longer period if required by the applicable country regulatory requirements.

If the responsible 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. The sponsor must be notified in writing of the name and address of the new custodian. Under no circumstance shall the investigator relocate or dispose of any study documents before having obtained written approval from the sponsor.

If it becomes necessary for the sponsor or the appropriate regulatory authority to review any documentation relating to this study, the investigator/institution must permit access to such reports.

The sponsor will archive study documents and study data electronically and as paper versions.

13.4 Notification requirements and time frames

The study may be subject to auditing activities by appropriate regulatory authorities. It is important that the Investigator and relevant study personnel are available during audits/inspections and that sufficient time is devoted to the process. Data requested by regulatory authorities have to be provided within the required time frames.

13.5 Corrective and preventive actions and principal investigator disqualification criteria

The Investigator and respective study personnel will be trained by the sponsor and/or 3M authorized representatives on study documentation to ensure the accuracy and completeness of the data reported in the eCRFs and other documents such as study diaries. The site monitor will verify that study records are adequately maintained and address necessary corrective actions if needed. Submission of knowingly false information from the Investigator to 3M or failure to comply with the study protocol and applicable regulations will disqualify the Investigator from the study**.**

13.6 Other aspects of clinical quality assurance

3M and authorized CRO are responsible for implementing and maintaining quality assurance and quality control systems through written standard operating procedures 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.

14. Deviations from clinical investigation plan

14.1 Amendments

The party initiating an amendment must confirm it clearly in writing using the Amendment/Administrative Revision Form of the ethics committee if applicable. 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 patients, the scope of the study or scientific quality.

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

14.2 Protocol Deviations

A protocol deviation is a departure from the protocol that will likely affect the safety, rights or welfare of patients, the scope of the clinical study or the scientific quality.
A protocol deviation is only for an individual patient. Each protocol deviation will be documented by completing a Protocol Deviation Case Report Form. This documentation will include the type of deviation and a description of the circumstances surrounding the deviation.

15. Device accountability

3M requires investigators to maintain accountability and adequate inventory security of the study device at all times. The investigator or designee will:

- Upon receipt of study device, check the contents and return the completed confirmation of receipt to the sponsor.
- Keep study device in a secure storage area, accessible only to authorized individuals.
- Dispense study device only to patients properly enrolled into the study.
- Return all unused study device to 3M at the end of the study, or dispose of as agreed upon.

16. Statement of compliance

This study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. All regional or national regulations will be followed, as appropriate. The study will not begin until the local Ethics Committees approved the study. Any additional requirements imposed by the Ethics Committees will be followed, if appropriate. The CE-marked study device will be used within its intended use. 3M recognizes its liability in law to compensate for any injuries sustained by patient participation in this study in accordance with the relevant guidelines of the countries where the study is conducted.

17. Informed consent process

The Investigator must ensure that written informed consent is obtained from the patient or patient's legally authorized representative before including any patient, and before conducting any study-related assessments. Informed consent may be given by the legally authorized representative only if a patient is unable to make the decision to participate in the study (e.g. seriously ill or unconscious patient, mentally ill person, mentally handicapped person). In such cases, the patient shall also be informed about the clinical study within his/her ability to understand. The Investigator must provide the prospective patient or the prospective patient's legally authorized representative, 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 patient and/or legally authorized representative all the information that he/she needs, 2) ensure that the patient and/or legally authorized representative understands the information and 3) give the patient and/or legally authorized representative a chance to consider study participation. The process should permit the patient and/or patient's legally authorized representative to ask questions and exchange information freely. Specifically, the Investigator is to explain to each patient and/or patient's legally authorized representative all elements of informed consent. After the explanation, the patient or legally authorized representative 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 patient or the patient's legally authorized representative. A signed and dated copy of the consent/assent form must be maintained in the Investigator Site File at all times. The informed consent process must be followed, and the patient's participation in the study, must be documented in the patient's medical record/chart.

17.1 Special circumstances for informed consent

17.1.1 Patient needing legally authorized representatives

Informed consent process is to be followed as described under 17.

17.1.2 Patient unable to read or write

If patient is unable to read or write an independent witness must be present throughout the process. The written informed consent form and any other information must be read aloud and explained to the prospective study participant or his/her legally authorized representative and, whenever possible, either must sign and personally dated the

informed consent form. The witness also signs and personally dates the informed consent form attesting that the information is accurately explained and that informed consent is freely given.

18. Adverse events, adverse device effects and device deficiencies

18.1 Assessment of safety

The study assesses the effects of a CE-marked device used within its intended use in comparison to hospital IAD standard care. Following the guidance of MEDDEV 2.12 rev 8 “Guidelines on a medical devices vigilance system” all incidents will be assessed and reported according to the reporting modalities of the national competent authorities. The national regulations and local requirements for clinical studies with CE-marked device will determine which safety issues are to be reported to the ethics committees/institutional review boards. Beside the regulatory framework, the sponsor defines the following safety documentation for this study: The principal measure of safety will be the occurrence and nature of serious adverse events probably or possibly related to the study device (i.e. serious adverse device effects) or hospital IAD care products used in this study. Additionally, all adverse events probably or possibly related to the study device (i.e. adverse device effects), the hospital IAD care products or the study procedures will be documented. Adverse events with direct effect on the skin assessment area are of interest and will be documented as well. Deficiencies of the study device with respect to its identity, quality, durability, reliability, safety or performance including malfunctions, use errors, and inadequate labelling are to be documented on a sponsor provided device deficiency form but not in the eCRF (meaning quality complaints and near incidents of the study device). This includes any discovery or malfunction or deterioration in the characteristics and/or performance of the study device, as well as any inadequacy in the labelling or in the instructions for use which might have led to a deterioration in the state of health of patient or user if the circumstances would have been less fortunate or the event would not have been prevented due to the timely intervention of health care personnel (all device deficiencies that led to any hazard for the patient have to be regarded as adverse device effect and are to be documented in the eCRF).

NOTE: Untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including an abnormal laboratory finding) in patients, users or other persons that are not linked to the products or procedures used in this study or do not directly affect the skin

assessment area are to be excluded from documentation including all internal diseases unless local regulations provide for this.

18.1.1 Safety parameters

The main safety parameters of this post-market IAD care study are the number and nature of serious adverse events possibly or probably related to the study device (i.e. serious adverse device effects) or to the IAD care products used in the comparative group.
Additionally, the number and nature of the following adverse events will be documented:
- adverse events probably or possibly related to the study device (i.e. adverse device effects)
- adverse events probably or possibly related to one of the IAD hospital care products
- adverse events probably or possibly related to one of the study procedures
- adverse events with direct effect on the skin assessment area. Examples are pressure ulcers or skin infections such as fungal/bacterial/viral infections within the skin area observed for this study.

All national and local requirements with regard to safety documentation will be considered for this study. Adverse events not mentioned in the list above will not be collected/analyzed during this study.

18.1.2 Assessment of methods

Safety parameters defined for this study will be collected for all study participants beginning at Day 01 until the final study visit, or until the patient is discharged from the hospital. The Adverse Event Case Report Form will be used to capture any safety-related concerns (eCRF). Device deficiencies regarding Cavilon Advanced Skin Protectant will be documented on the Device Deficiency Form (i.e. quality complaints and near incidents). The Device Deficiency Form is stored in the Investigator Site File. All device deficiencies that led to any hazard for the patient have to be regarded as adverse device effect and are to be documented in the eCRF/Adverse Event Case Report Form.

18.2 Foreseeable adverse events and anticipated adverse device effects

An allergic reaction to any of the ingredients of Cavilon Advanced Skin Protectant would constitute an anticipated adverse event according to the manufacturer's instructions for use.

18.3 Definitions

The definitions given in this section are the official definitions of the ISO 14155:2011 "Clinical investigation of medical devices for human subjects – good clinical practice". The standard addresses good clinical practice for clinical investigation to assess the safety or performance of non-CE marked devices but the principles set forth in this standard also apply to all other clinical investigations and should be followed as far as possible, considering the nature of the clinical study and the requirements of national regulations.

Adverse Device Effect

Adverse event related to the use of an investigational medical device.
NOTE 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.
NOTE 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.

Adverse Event

Any untoward medical occurrence, unintended disease or injury, or any untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device.
NOTE 1: This definition includes events related to the investigational medical device or the comparator.
NOTE 2: This definition includes events related to the procedures involved.
NOTE 3: For users or other persons, this definition is restricted to events related to investigational medical devices.

Device Deficiency

Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance
NOTE: Device deficiencies include malfunctions, use errors, and inadequate labelling.

Serious Adverse Event

Adverse event that:
a) led to death,
b) led to serious deterioration in the health of the subject that either:
1) resulted in a life-threatening illness or injury, or
2) resulted in a permanent impairment of a body structure or a body function, or
3) required in-patient or prolongation of existing hospitalization, or
4) resulted in medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function.
c) led to fetal distress, foetal death or a congenital abnormality or birth defect.

NOTE: Planned hospitalization for a pre-existing condition, or a procedure required by the Clinical Investigation Plan, without a serious deterioration in health, is not considered a serious adverse event.
NOTE: This includes device deficiencies that might have led to a serious adverse event if a) suitable action had not been taken or b) intervention had not been made or c) if circumstances had been less fortunate. These are handled under the SAE reporting system.

Serious Adverse Device Effect

Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

18.4 Reporting and timelines

18.4.1 Reportable events

Incidents will be reported to the national competent authorities. According to MEDDEV 2.12. rev 8 an incident is defined as any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labeling or the instructions for use which, directly or indirectly, might lead to or might have led to the death of a patient, or user or of other persons or to a serious deterioration in their state of health.
According to MEDDEV 2.12 rev 8 a serious deterioration in state of health can include (non exhaustive list):
a) life-threatening illness
b) permanent impairment of a body function or permanent damage to a body structure,
c) a condition necessitating medical or surgical intervention to prevent a) or b).
Examples:
- clinically relevant increase in the duration of a surgical procedure,
- a condition that requires hospitalization or significant prolongation of existing hospitalization.
d) any indirect harm as a consequence of an incorrect diagnostic or IVD test result or as a consequence of the use of an IVF/ART device when used within manufacturer's instructions for use
e) fetal distress, fetal death or any congenital abnormality or birth defect

The national regulations and local requirements for clinical studies with CE-marked device will determine which safety events are to be reported to the ethics committees/institutional review boards.

18.4.2 Report by whom

Incidents related to the study device will be reported by the 3M safety officer to the applicable national competent authorities. Incidents in relation to one of the hospital IAD care products are to be reported by the hospital to the respective manufacturer and to the national competent authorities.
National regulations and local requirements of the ethics committees/institutional review

boards will define which events are to be reported by whom.

18.4.3 Report to whom

Incidents will be reported to the applicable national competent authorities. National regulations and local requirements of ethics committees/institutional review boards will define which events are to be reported.

18.4.4 Report by the investigator to the sponsor

The investigator shall report immediately (max. 24 hours) to the sponsor all serious adverse events that are probably or possibly related to one of the products or procedures of the study. In addition, the investigator shall report all device deficiencies that could have been resulted in a serious deterioration in the health of the patient or user if the circumstances would have been less fortunate or were not prevented due to the timely intervention of health care personnel (near incident). Furthermore, all emergency deviations from the protocol are to be reported to the sponsor within 24 hours and have to be documented in the Protocol Deviation Form of the eCRF. The sponsor's Medical Monitor is to be informed immediately by phone and Email about the occurrence of any of the events described above. For all related serious adverse events (i.e., serious adverse device effects) the Adverse Event Form of the eCRF has to be filled out as soon as possible since an alert email is sent automatically by the EDC system to the sponsor's Medical Monitor. Device deficiencies that could have been resulted in a serious event are to be documented on the device deficiency form and forwarded to the sponsor's Medical Monitor as an attachment. The 3M Monitor should be cc'd to secure the communication flow in case the 3M Medical Monitor is not immediately available for any reason.

18.4.5 Reporting form

Reportable events must be reported using the official forms featured by the national competent authorities and ethics committees/institutional review boards on their websites if applicable.

18.5 Emergency contact details

3M Medical Monitor:

[redacted]

18.6 Drug Monitoring Committee

Not applicable for this study

19. Suspension or premature termination of the clinical investigation

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 participants
- Failure of the Investigator to comply with regulations
- Insufficient adherence to protocol requirements
- Failure of the Investigator to enroll patients into the study at an acceptable rate
- Submission of knowingly false information from the Investigator to 3M
- Withdrawal of EC approval
- A decision on the part of 3M to suspend or discontinue evaluation of the study device

20. 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.

21. Data handling and record keeping

21.1 Site personal

Prior to study initiation, the Investigator must provide 3M with a signed Investigator Agreement. 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 regulations.

21.2 Pre-clinical investigation documentation requirements

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

a) Signed protocol including any amendments in place prior to study initiation

b) Curriculum vitae for the Investigator and any Co-Investigators

c) Ethics committee approved informed consent form

d) Ethics committee study approval letter

e) Ethics committee name, location and chairperson

g) Signed Investigator Agreement with regard to the clinical study

21.3 Completion and return of case report forms

Once the electronic forms are completed by the Investigator or study nurse, the monitor will review the information to ensure completeness and consistency and to ensure adequate quality control and assurance of patient data. Any discrepancies found during CRF review are to be clarified by the Investigator or study nurse. After the study the investigator will receive an USB stick or CD with all CRFs in PDF format extracted from the electronic Data Capture System.

22. Final report

3M will prepare a Sponsor Final Report and submit the document to all reviewing Ethics Committees, if required.

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24. Appendix

NOTE: After IAD healing, the recurrence of IAD in both study groups is to be examined. If the hospital routinely does not use IAD prevention products, the recurrence of IAD is still to be observed for the group allocated to hospital IAD standard care. In this case, the study procedures of “Application: Comparator” and “Pain Score: Application” no longer apply (Appendix 24.1 B).

24.1 Clinical investigational schedule

A) Patients allocated to Cavilon Advanced Skin Protectant

Assessment	IC	D01	D02	D03	D04	D05	D06	D07	D08	D09	D10	D11	D12	D13	D14	D15	D16	D17	D18	D19	D20	End of Study (D21 or discontinuation)
Informed Consent (IC)	X																					
Inclusion/Exclusion		X																				
Randomization		X																				
Demographics		X																				
IAD History		X																				
Medications		X																				
Barthel Index		X																				
Braden Scale		X																				
Skin Cleansing		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pain Score: Cleansing		X			X			X			X			X			X			X		X
IAD Nursing Time					X																	
Skin Assessment (Diary)		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Photography		X			X			X			X			X			X			X		X
Application: Study Device		X			X			X			X			X			X			X		
Pain Score: Application		X			X			X			X			X			X			X		
Tracking IAD Care (Diary)		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
IAD Product Specification		X	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)
Adverse Events		(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)
Protocol Deviation		(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)
End of Study Form																						X

(x) = if applicable

B) Patients allocated to hospital IAD standard care

Assessment	IC	D01	D02	D03	D04	D05	D06	D07	D08	D09	D10	D11	D12	D13	D14	D15	D16	D17	D18	D19	D20	End of Study (D21 or discontinuation)
Informed Consent (IC)	X																					
Inclusion/Exclusion		X																				
Randomization		X																				
Demographics		X																				
IAD History		X																				
Medications		X																				
Barthel Index		X																				
Braden Scale		X																				
Skin Cleansing		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pain Score: Cleansing		X			X			X			X			X			X			X		X
IAD Nursing Time					X																	
Skin Assessment (Diary)		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Photography		X			X			X			X			X			X			X		X
Application: Comparator *		X	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	
Pain Score: Application		X			X			X			X			X			X			X		
Tracking IAD Care (Diary)		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
IAD Product Specification		X	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)
Adverse Events		(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)
Protocol Deviation		(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)
End of Study Form																						X

* Hospital IAD standard care: skin protectant building up the moisture barrier or IAD wound dressing. The application frequency varies depending on the product.
(x) = if applicable

24.2 Ghent Global IAD Categorization Tool

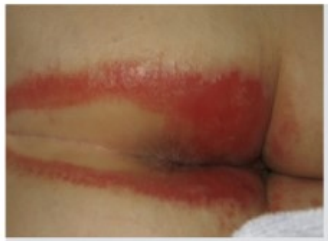
IAD 1A and IAD 2A

GLOBIAD

Ghent Global IAD Categorisation Tool

Category 1: Persistent redness

1A - Persistent redness without clinical signs of infection



Critical criterion

- Persistent redness
  A variety of tones of redness may be present.
  Patients with darker skin tones, the skin may be paler or darker than normal, or purple in colour.

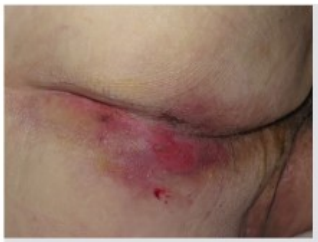
Additional criteria

- Marked areas or discolouration from a previous (healed) skin defect
- Shiny appearance of the skin
- Macerated skin
- Intact vesicles and bullae
- Skin may feel tense or swollen at palpation
- Burning, tingling, itching or pain may be present

1A

Category 2: Skin loss

2A - Skin loss without clinical signs of infection



Critical criterion

- Skin loss
  Skin loss may present as skin erosion, denudation, excoriation, open vesicles, or open bullae.
  The skin damage pattern may be diffuse.

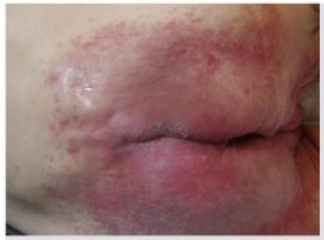
Additional criteria

- Persistent redness
  A variety of tones of redness may be present. Patients with darker skin tones, the skin may be paler or darker than normal, or purple in colour
- Marked areas or discolouration from a previous (healed) skin defect
- Shiny appearance of the skin
- Macerated skin
- Intact vesicles and bullae
- Skin may feel tense or swollen at palpation
- Burning, tingling, itching or pain may be present

2A

IAD 1B and IAD 2B

1B - Persistent redness with clinical signs of infection



Critical criteria

- Persistent redness
  A variety of tones of redness may be present. Patients with darker skin tones, the skin may be paler or darker than normal, or purple in colour
- Signs of infection
  Such as satellite lesions (eg pustules or maculopapular rash) or white scaling of the skin (indicating a fungal infection eg Candida albicans)

Additional criteria

- Marked areas or discolouration from a previous (healed) skin defect
- Shiny appearance of the skin
- Macerated skin
- Intact vesicles and bullae
- The skin may feel tense or swollen at palpation
- Burning, tingling, itching or pain may be present

1B

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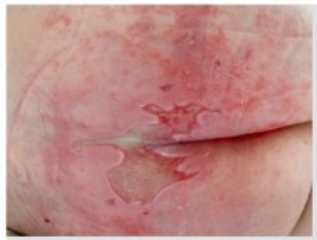
2B - Skin loss with clinical signs of infection



Critical criteria

- Skin loss
  Skin loss may present as skin erosion, denudation, excoriation, open vesicles, or open bullae. The skin damage pattern may be diffuse.
- Signs of infection
  Such as satellite lesions (eg pustules or maculopapular rash), white scaling of the surrounding skin or in the wound bed (indicating a fungal infection eg Candida albicans), slough visible in the wound bed (yellow/brown/greyish), green appearance within the wound bed (indicating a bacterial infection eg Pseudomonas aeruginosa), excessive exudate levels, purulent exudate (pus) or a shiny appearance of the wound bed.

Additional criteria

- Persistent redness
  A variety of tones of redness may be present. Patients with darker skin tones, the skin may be paler or darker than normal, or purple in colour
- Marked areas or discolouration from a previous (healed) skin defect
- Shiny appearance of the skin
- Macerated skin
- Intact vesicles and bullae
- Skin may feel tense or swollen at palpation
- Burning, tingling, itching or pain may be present

2B

Beeckman D, Van den Bussche K, Beele H, Ciprandi G, Coyer F, De Meyer D, Dunk AM, Fouri A, García-Molina P, Gray M, Johansen E, Karadağ A, Kis Dadara Z, Meaume S, Pokorna A, Romanelli M, Ruppert S, Schoonhoven L, Smet S, Steininger A, Stockmayr M, Van Damme N, Voegeli D, Verhaeghe S, Van Hecke A, Kottner J. (2017). Development and Clinical Validation of the Ghent Global IAD Categorisation tool (GLOBIAD). In progress.