NCT #: NCT04906512

Study Title	A Randomized Perspective, Open and Parallel Controlled Study Comparing 3M Tegaderm CHG I.V. Securement Dressing with 3M Tegaderm Transparent Dressing for Evaluation of Antimicrobial Efficacy on DVC Insertion Site in Adult in Critical Care
Study Number	EM-05-014894
Release Date	04/05/2021 11:40:57 PM CDT
Name of Device Under Investigation	3M Tegaderm CHG I.V. Securement Dressings
Sponsor Address	3M China
Manufacturer Address	3M Company

ELECTRONIC SIGNATURES:

Signer	Role	Date Signed
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Investigator Statement

Statements of Compliance

This clinical investigation shall be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki.

This clinical investigation shall be conducted in accordance with ISO-14155:2011 and future versions, US FDA 21 CFR parts 812, 50, 54, 56, and any regional or national regulations, as appropriate.

The clinical investigation shall not begin until the required approval/favorable opinion from the Institutional Review Board (IRB)/Ethics Committee (EC) and regulatory authority (if applicable) has been obtained and permission to proceed has been received from the study Sponsor. Any additional requirements imposed by the IRB/EC or regulatory authority shall be followed.

I have read the Clinical Investigation Plan (CIP), including all appendices, as well as supporting study related documents and I agree that it contains all necessary details for me and my staff to conduct this study as described. I agree to record all adverse events/ deviations and report those adverse events/ deviations to the Sponsor per this CIP and IRB/EC per local requirements. I always agree to maintain product accountability and ensure security of study materials. I agree to comply with financial disclosure requirements.

All subjects will sign and date the approved Informed Consent before any study procedures are conducted, as applicable

I will ensure that all subjects meet inclusion criteria before enrolling them in the study.

I agree to maintain and retain records as required by this Clinical Investigation Plan.

Investigator's Signature:	
Investigator's Name:	Hongping Qu
Institution:	Shanghai Ruijin Hospital
Date of Signature:	

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1.0 SYNOPSIS

Study Title	A Randomized Perspective, Open and Parallel Controlled Study Comparing 3M Tegaderm CHG I.V. Securement Dressing with 3M Tegaderm Transparent Dressing for Evaluation of Antimicrobial Efficacy on DVC Insertion Site in Adult in Critical Care
Study Type	post-market
Principal Investigator (PI)	**Name**: Hongping Qu **Title:** Professor **Site:** Ruijin Hospital Critical Care Department
Device under Investigation Summary	3M Tegaderm CHG I.V. Securement Dressings This product is composed of a transparent dressing and a gel pad. The gel pad contains 2% (w/w) chlorhexidine gluconate (CHG), which is an antimicrobial agent. This product is suitable for covering and protecting catheter sites (including arterial and venous catheters, intravascular catheters, and percutaneous devices) on the body surface and securing devices to healthy skin. This product should not be used on infected wounds or unhealthy skins.
Sponsor	3M China
Purpose	The objective of this study is to evaluate the antimicrobial efficacy of Tegaderm CHG dressing on DVC insertion site in adult patients in critical care
Design	This is a single-center, prospective, randomized controlled clinical trial designed to compare the antimicrobial efficacy of Tegaderm CHG I.V. Securement Dressing and transparent dressings for deep vein catheterization in adult ICU patients. Considering the easy-to-distinguish appearances of both products used, this trial will adopt an open-label design. The primary endpoint is the rate of CVC tip colonization (positive catheters after culture/total catheters). Subjects eligible for enrollment will be randomly assigned to either the Tegaderm CHG dressing group or the transparent dressing group, and patients in both groups will be given catheterization according to the hospital's standards and nursed according to the catheter maintenance procedure. The investigator would monitor the subjects during dressing changes, observing the subjects' general conditions, skin condition at the DVC site and the dressing condition, and change a dressing or take relevant measures (if

	applicable), until the end of the trial, i.e. CVC removal or patient transfer out of the ICU.
Selection of Subjects	440 subjects who meet the inclusion/exclusion criteria will be enrolled. Subjects will be adult voluntary clinical subjects, of either sex, at least 18 years of age, who are ICU patients undergoing deep venous catheterization (DVC), in which a CVC catheter must be used while other types of catheters such as hemodialysis, PICCO, and floating catheters may be used concurrently. Inclusion Criteria: Subjects may be included that meet the following criteria: 1. Subjects should be at least 18 years old or older at the time of providing consent; 2. Subjects would be available to attend all visits required in the trial, be inpatients in the Department of Critical Care Medicine and have an expected length of stay in the ICU of no less than 3 days; 3. The subject or his/her legally authorized representative should be competent to sign the informed consent form; 4. The patient must have a central venous catheter (CVC) used on him/her, which may or may not be used in combination with other types of DVCs; 5. The patient's catheter insertion site is free of deformities, phlebitis, infiltrations, dermatitis, eczema, rashes, breaks, burns, tattoos or other skin conditions that may affect the integrity of the skin at the insertion site; 6. The patient would comply with the DVC treatment process and the nursing process prescribed in this protocol. Exclusion Criteria: Subjects may not be included that meet any of the following criteria: 1. The subject is unwilling/unable to attend study visits (unlike IC);

	2. There is sunburn, skin infection or scar, mole or other blemishes on the subject's catheterization site that would affect the scoring or measurement of the site; 3. The patient is assessed by the investigator as being at high risk of CLABSI, or known to be CLABSI, based on the environment, duration, and site conditions of catheterization; 4. The patient is documented or known to have allergies (sensitivities) to adhesive products, or other products involved in the trial, e.g. transparent dressings, CHG and alcohol; 5. The patient is being or has been subjected to other antibiotic, catheter or skin-related clinical trials; 6. The patient needs topical application of creams containing antimicrobial ingredients or other antimicrobial fluids beneath the Tegaderm CHG dressing or transparent dressing for skin disinfection, in addition to the requirements of this protocol; 7. The patient is assessed by the investigator as being at high risk of blood stream infection, or known to be sepsis, caused by blood stream infection; 8. The patient has dermatitis, burns, lesions, breaks, eczema, tattoos or other conditions at the catheter insertion site that would interfere with observation in the trial; 9. Women who are pregnant or breast feeding; 10. Patients who are not eligible for the study at the discretion of other investigators.
Device Regulatory Classification	The test device is imported Class II medical device with the license of GXZJ No.20163642045. The control device is imported Class II medical device with the license of GXZJ No.20182642129. Both have been registered in China.

Primary Objective(s)	The primary objective of this study is compare the difference in the bacterial colonization rate at the CVC tip and the catheterization site on the skin after removal (number of culture-positive cases/total catheters × 100%) between the test and control groups
Secondary Objective(s)	The secondary objective of this study is to compare the differences in the following indicators between the test and control groups: • Number of positive cases per 1,000 catheter-days of bacterial colonization at CVC tips • Bacterial colonization rate at the tip of other types of (percutaneous) deep vein catheters and the catheterization site (number of culture positive cases/total catheters x 100% and number of positive cases per 1,000 catheter-days), including hemodialysis, PICCO, float catheters, etc. • Incidence rate of Central Line Associated Bloodstream Infections (CLABSI) or Catheter Related Blood Stream Infections (CRBSI) • Type of pathogenic microorganism (G+/G-/fungal or specific species, drug-resistant bacteria, etc.) and percentage of positivity • Securement performance of the dressing: Frequency of dressing changes associated with wear time and lift or drop-off • Effects on the skin of the covered area, e.g. local infection, local skin irritation
Endpoint(s)	The primary endpoint is the removal of the CVC from the patient with deep vein catheterization to perform catheter-tip culture and sampling and culture of bacteria from the skin around the insertion site. Secondary endpoints 1. Removal of other types of DVCs, such as hemodialysis and PICCO to perform catheter-tip culture and sampling and culture of bacteria from skin around the insertion site; 2. Occurrence of suspected CLABSI/CRBSI, performing catheter-tip culture and blood bacterial culture;

	3. Dressing securement performance, such as lift or drop-off; 4. Safety indicators, mainly referring to the effect of the dressing on the state of the skin.
Randomization	Subjects are randomly assigned to test device group or control device group
Duration of the Study	The duration of the study is anticipated to be 15 months from First Subject In to Last Subject Out. The duration of each study subject's participation will be 3-14 days, depending on the subject's disease treatment schedule, each study subject would be treated with the same CVC for essentially no more than 2 weeks
Sponsor Study Contact	**Name:** Yang Ye **Address:** 222 Tianlin Road, Xuhui District, Shanghai **Telephone:** 18018588001 **Email:** yye2@mmm.com
Medical Monitor Contact	**Name:** Matthew Cooper, MD MBA FACS **Address:** 3M US **Telephone:** +16517364689 **Email:** mmcooper2@mmm.com

2.0 BACKGROUND AND JUSTIFICATION

Use of deep venous catheters (DVC) in ICU patients, such as central venous catheters (CVC), pulse index continuous cardiac output (PICCO) catheters and hemodialysis catheters is associated with a high risk of bloodstream infections. It is estimated that approximately 3-5% of catheterization processes would trigger catheter-related bloodstream infections CRBSI[1] (Moureau et al, 2009). The World Health Organization (WHO), the National Institute for Clinical Excellence (NICE) and the Centers for Disease Control (CDC) all recommend the use of chlorhexidine-impregnated dressings to reduce the risk of CRBSI. Several clinical trials have proved the clinical efficacy of chlorhexidine-impregnated dressings in reducing CRBSI and/or CLABSI. [2,3,4]

The patient's skin flora is one of the main sources of microbial pathogens, and microorganisms can migrate from the CVC insertion site along the outer surface of the catheter and hematogenously spread from other infected sites or contaminated infusion sites, contaminating the center of the catheter and resulting in bacterial colonization[10,11]. CHG-impregnated dressings can maintain low skin microbial counts at the securement site during use. CHG has long been used as a skin disinfectant and antimicrobial agent, but challenges have arisen as the skin microbiota begins to regenerate a few hours after disinfection. A study[12] shows that Tegaderm CHG dressing significantly reduced the number of microorganisms at the CVC insertion site, suture site and catheter colonization. Several studies have demonstrated that the use of Tegaderm CHG dressings facilitates easy visualization of the catheterization site and that the risk of adverse skin reactions is no higher than existing comparable products[5-9]. In addition, the NICE's advisory committee has concluded that Tegaderm CHG dressings offer greater finished product benefits compared to chlorhexidine-free dressings.

Tegaderm CHG Dressing is used to cover and protect the catheterization site on the body surface and to secure devices to skin. Tegaderm CHG Dressing is indicated to reduce skin bacterial colonization and catheter bacterial colonization, inhibit microbial regeneration, and reduce the rate of central catheter-related bloodstream infections (CRBSI). Tegaderm CHG Dressing consists of a transparent dressing and a gel pad. The gel pad contains 2% (w/w) chlorhexidine gluconate (CHG). CHG is a classical germicide with broad-spectrum antibacterial and antifungal activity. The transparent dressing acts as a barrier to protect the venipuncture site, effectively blocking external contamination, including fluids (waterproof), bacteria, virus and fungi. In vitro tests have demonstrated that the Tegaderm CHG gel pad in the dressing can inhibit a wide range of Gram-positive/negative bacteria and yeasts. Tegaderm CHG dressings are transparent for continuous observation of the puncture site and are breathable to allow moisture to escape.

Although many studies support the clinical efficacy of Tegaderm CHG dressing in reducing skin and catheter bacterial colonization, to our knowledge, no similar studies have been conducted in China to date to verify its clinical efficacy. Therefore, 3M plans to conduct a study in China aimed at exploring the clinical efficacy of Tegaderm CHG dressings in inhibiting bacterial colonization at CVC tips in the current clinical practice and healthcare environment in China.

This trial will follow the applicable principles in the Declaration of Helsinki and the Chinese Medical Device GCP Order No.25 (2016).

2.1 Description of Study Device

3M™ Tegaderm™ CHG I.V. Securement Dressing consists of a transparent dressing and a gel pad. The gel pad contains 2% (w/w) chlorhexidine gluconate (CHG). CHG is a classical germicide with broad-spectrum antibacterial and antifungal activity. The transparent dressing acts as a barrier to protect the venipuncture site, effectively blocking external contamination, including fluids (waterproof), bacteria, virus and fungi.

In vitro tests have demonstrated that: The transparent film of Tegaderm CHG dressing can block viruses of up to 27nm or larger diameter in intact and unbroken conditions. The barrier to viruses is based on the physical properties of the dressing, rather than the auxiliary properties of CHG.

In vitro tests for germicidal time and inhibition zone proved that: The gel pad in Tegaderm CHG dressing is inhibitory to a wide range of gram-positive/negative bacteria and yeasts. Tegaderm CHG dressings are transparent for continuous observation of the puncture site and are breathable to allow moisture to escape.

The control product is a CHG-free transparent dressing used to cover and protect the catheterization site on the body surface and to secure the device to the skin, without any antibacterial ingredients, which is the currently most commonly used transparent dressing in DVC care in China.

3.0 STUDY DEVICE INFORMATION

Trial product

Working principle:

The primary purpose of 3M™ Tegaderm™ CHG I.V. Securement Dressing is to secure devices to skin; and secondly, the dressing contains an antimicrobial ingredient that inhibits microbial regeneration. This product is used to cover and protect the catheter sites on the body surface and to secure devices to skin and is available in a variety of models and sizes.

Product model: 1657R, 1658R, 1659R, 1660R

Size: 1657R, 8.5 cm x 11.5 cm (3-12 in x 4-1/2 in);

1658R, 10 cm x 12 cm (4 in x 4-3/4 in);

1659R, 10 cm x 15.5 cm (4 in x 6-1/8 in);

1660R, 7 cm x 8.5 cm (2 3/4 in. x 3 3/8 in)

The average CHG content (mg of CHG contained in the gel pad) of a single piece of dressing: 45 mg for both 1657R and 1658R; 78 mg for 1659R and 15 mg for 1660R.

Product usage

3M™ Tegaderm™ CHG Chlorhexidine Gluconate I.V. Securement Dressings is used to cover and protect catheter sites and to secure devices to skin.

Indications

The product is suitable for covering and protecting catheterization sites (covering arterial and venous catheters, intravascular catheters and percutaneous devices) on the body surface and securing the device to healthy skin. This product should not be used on infected wounds or unhealthy skins.

Contraindications

1. Do not use on patients with known hypersensitivity to chlorhexidine gluconate or alcohol;
2. Do not use at catheter insertion sites with dermatitis, burns, lesions or tattoos.

Warning

1. Use on infants with caution.
2. For external use only. Do not contact the product with ears, eyes, mouth or mucous membranes.

Precautions

1. The product shall not be used on broken wounds or unhealthy skin.
2. The product shall not be re-sterilized by gamma, electron beam or steam.
3. The skin must be dry and free of soap and hand sanitizer residue to prevent skin irritation and ensure good adhesion.

Possible adverse reactions associated with chlorhexidine gluconate

1. Occasionally, it can cause contact dermatitis. Highly concentrated solutions are highly

irritating to the eyes and conjunctiva.

2. Rare cases of local irritation and allergic reactions have been reported.
3. Children who accidentally eat it may develop symptoms of alcohol poisoning (e.g. slurred speech, drowsiness, wobbly gait, etc.) and there should be no delay in emergency medical treatment.

Control product

3M™ Tegaderm™ Transparent Film Dressing 1626W

Working principle

The main purpose is to secure devices to skin.

Product features

Transparent dressing, i.e. CHG-free transparent dressing, can be used to cover and protect catheter sites on the body surface and to secure devices to skin, without any antibacterial ingredients, and are the currently most commonly used transparent dressings in DVC care in China.

Product usage

The product is used to cover and protect catheter sites on the body surface and to secure devices to skin.

Indications

It can be used to cover and protect catheter sites and wounds, maintain a moist environment, and also be used as a secondary dressing to cover those areas of skin susceptible to damage or abrasions or to secure devices.

Contraindications

There are no known contraindications.

Warning:

1. This product shall not be used as a substitute for sutures and other primary wound closures.
2. This product shall not be used on infected catheter sites or infected wounds.

Precautions

1. Apply dressing until bleeding has stopped.

2. The dressing shall not be stretched during application, as tension can cause skin trauma.

3. The skin must be dry and free of soap and hand sanitizer residue to prevent skin irritation and ensure good adhesion.

4. Dressings shall not be re-sterilized by gamma, electron beam or steam.

5. Antibacterial ointments containing polyethylene glycol may disrupt the strength of the film.

6. This dressing may be used on infected areas only under the care of a healthcare professional.

Table 3.0-1: Device Information

Name of device	Model
3M™ Tegaderm™ CHG I.V. Securement Dressing	1657R, 1658R, 1659R, 1660R
3M™ Tegaderm™ Transparent Dressing	1626W

3.1 Device Regulatory Classification

The test device is imported Class II medical device with the license of GXZJ No.20163642045. The control device is imported Class II medical device with the license of GXZJ No.20182642129. Both have been registered in China.

3.2 Intended Use of Device

The subject device 3M™ Tegaderm™ CHG I.V. Securement Dressing is used to cover and protect catheter sites and to secure devices to skin.

The control product transparent dressing is used to cover and protect catheter site on the body surface and secure devices to skin.

Both products are used in accordance with the hospital's catheterization standard and catheter line maintenance procedure.

3.3 Risks and Benefits of the Device(s) Used in this Study

3.3.1 Risks of the Device

Dressings are considered to be low-risk medical devices and are commonly used in health care and at home with few problems reported. Potential risks to subjects include possible localized skin irritation: such as itching, erythema and rash, some minor pain and erythema during removal, contact dermatitis and systemic allergic reactions, and skin stripping without any long-term effect. If the investigator discovers any erythema symptom equal to or greater than Grade 3 (0-4 scale; see Appendix B for grading details), or if any allergic reaction occurs, its use shall be discontinued for that subject.

3.3.2 Anticipated Adverse Device Effects

Skin and subcutaneous tissue reactions/allergies:

1. Dryness/damage
2. Rash, irritation, blisters
3. Pruritus/itching
4. Excoriation/skin ulceration
5. Skin peeling
6. Skin scarring in the case of significant skin irritation
7. Skin maceration
8. Hyperpigmentation/hypopigmentation in and/or around the area of dressing application
9. Erythema/redness, edema, inflammation or swelling in and/or around the area of dressing application

Mild discomfort:

1. Sweating due to the use of dressings
2. Abnormal sensations (numbness, tingling, prickle, formication)

Possible adverse reactions associated with chlorhexidine gluconate

1. Occasionally, it can cause contact dermatitis. Highly concentrated solutions are highly irritating to the eyes and conjunctiva.
2. Rare cases of local irritation and allergic reactions have been reported.
3. Children who accidentally eat it may develop symptoms of alcohol poisoning (e.g. slurred speech, drowsiness, wobbly gait, etc.) and there should be no delay in emergency medical treatment.

Others:

1. Local infection
2. Limited mobility/movement
3. Poor securement causing catheter to partially slip out
4. Systemic reactions (caused by allergic reactions to the dressing)

3.3.3 Residual Risks

Residual Risks of using tape over a long period or with multiple applications, subjects may develop sensitivity to the adhesives used in these products. Hypo/hyper pigmentation, etc.

3.3.4 Risk of Interactions with Concomitant Medical Treatments

There is minimal risk of interactions with any medical treatments the study subjects would receive as part of standard medical treatment.

3.3.5 Mitigation of Risk

Risk related to the device may be mitigated or controlled through appropriate selection of study subjects for inclusion into this study, adherence to this Clinical Investigation Plan, and reporting of Adverse Events, Device Deficiencies and deviations to the Sponsor. If the subject experiences any discomfort, the

investigators could discontinue the clinical trial and conduct appropriate treatment and care based on clinical judgment.

3.3.6 Benefits of the Device

There is no guarantee of benefits. However, several overseas studies support the clinical efficacy of Tegaderm CHG dressings in reducing bacterial colonization on skin and catheters.

3.3.7 Risk to Benefit Rationale

Based on the risks and benefits listed above, and according to this clinical study protocol, the subjects will not face a greater risk of harm than those who do not participate in this study because the control product is what is used in the treatment that subjects would receive if they did not participate in this study. And both the test product and the control product are commonly used in hospitals.

4.0 DESIGN OF CLINICAL INVESTIGATION

4.1 Design

This clinical trial is designed as a prospective, randomized, open-label, parallel-group controlled trial.

4.1.1 Scientific Rationale for Design

The control device has been commonly used for DVC securement in clinical institutions in China and is a routine product used in clinical trial centers.

This is an open-label trial, and because there are visible differences in the outer packaging and appearance of the devices used in two groups, it would be impossible to blind either the investigators or the subjects.

4.1.2 Minimization of Bias

The following measures have been taken to minimize or avoid bias in this study:

- Randomization: The random assignment gives each subject an equal chance of being assigned to either the test or control group without being influenced by the subjective intention of the investigator and/or the subject, allowing for a balanced distribution of multiple influence factors and avoiding selection bias or information bias as much as possible. This trial will use a random assignment approach to reduce bias due to sampling difference. After investigators confirm and verify the inclusion and exclusion criteria, eligible subjects will be randomly assigned to either the test group or the control group to receive treatment. The random number table is generated by a biostatistician using a program before the first enrollment.
- Parallel-group control: A parallel-group controlled approach is used in the trial design. Treatment of both test and control groups will be conducted concurrently so that factors that may affect the validity assessment are evenly distributed between the two groups.

5.0 OBJECTIVES OF THE CLINICAL INVESTIGATION PLAN

5.1 Primary Objective(s)

The primary objective of this study is compare the difference in the bacterial colonization rate at the CVC tip and the catheterization site on the skin after removal (number of culture-positive cases/total catheters × 100%) between the test and control groups.

5.2 Secondary Objective(s)

The secondary objective of this study is to compare the differences in the following indicators between the test and control groups:

- Number of positive cases per 1,000 catheter-days of bacterial colonization at CVC tips
- Bacterial colonization rate at the tip of other types of (percutaneous) deep vein catheters and the catheterization site (number of culture positive cases/total catheters x 100% and number of positive cases per 1,000 catheter-days), including hemodialysis, PICCO, float catheters, etc.

- Incidence rate of Central Line Associated Bloodstream Infections (CLABSI) or Catheter Related Blood Stream Infections (CRBSI)
- Type of pathogenic microorganism (G+/G-/fungal or specific species, drug-resistant bacteria, etc.) and percentage of positivity
- Securement performance of the dressing: Frequency of dressing changes associated with wear time and lift or drop-off
- Effects on the skin of the covered area, e.g. local infection, local skin irritation.

5.3 Endpoint(s)

5.3.1 Primary Endpoint(s)

The bacterial colonization rate at the CVC tip and the catheterization site on the skin after removal (number of culture-positive cases/total catheters × 100%)

The primary endpoint is the removal of the CVC from the patient with deep vein catheterization to perform catheter-tip culture and sampling and culture of bacteria from the skin around the insertion site.

5.3.2 Secondary Endpoint(s)

Removal of other types of DVCs, such as hemodialysis and PICCO to perform catheter-tip culture and sampling and culture of bacteria from skin around the insertion site;

Occurrence of suspected CLABSI/CRBSI, performing catheter-tip culture and blood bacterial culture;

Dressing securement performance, such as lift or drop-off;

Safety indicators, mainly referring to the effect of the dressing on the state of the skin.

6.0 POPULATION AND DURATION

The study will include 440 study subjects. The study will be conducted simultaneously in two ICU wards of Shanghai Ruijin Hospital.

The overall study is expected to last a total of 15 months. Depending on the subject's disease condition and treatment schedule, each subject's treatment duration with the same deep vein catheter is essentially no more than 2 weeks, so their participation in the study will last for approximately 3-14 days.

7.0 ENROLLMENT CRITERIA

Subjects enrolled in this clinical study must meet all the inclusion criteria and none of the exclusion criteria, as listed in the sections below.

7.1 Inclusion Criteria

Subjects may be included that meet the following criteria:

Table 7.1-1: Inclusion Criteria

Number	Inclusion Criteria
IC - 1	The subject is 18 years old or older at the time of providing consent.
IC - 2	The subject will be available to attend all visits required in the trial and have an expected length of stay in the ICU no less than 3 days.
IC - 3	The subject or his/her legally authorized representative is competent to sign the informed consent form
IC - 4	The patient must have a central venous catheter (CVC) used on him/her, which may or may not be used in combination with other types of DVCs
IC - 5	The patient's catheter insertion site is free of deformities, phlebitis, infiltrations, dermatitis, eczema, rashes, breaks, burns, tattoos, or other skin conditions that could affect the integrity of the skin at the insertion site
IC - 6	The patient will comply with the DVC treatment process and the nursing process prescribed in this protocol

7.2 Exclusion Criteria

Subjects must be excluded from participating in this study if they meet any of the following criteria:

Table 7.2-1: Exclusion Criteria

Number	Exclusion Criteria
EC - 1	The subject is unwilling/unable to attend the study visits. (Different from IC)
EC - 2	There is sunburn, skin infections or scars, moles or other blemishes on the subject's catheter site that would affect the scoring or measurement of the test site
EC - 3	The patient is assessed by the investigator as being at high risk of CLABSI, or known to be CLABSI, based on the environment, duration, and site conditions of catheterization
EC - 4	The patient is documented or known to have allergies (sensitivities) to adhesive products, or other products involved in the trial, e.g. transparent dressings, CHG and alcohol
EC - 5	The patient is being or has been subjected to other antibiotic, catheter or skin-related clinical trials
EC - 6	The patient needs topical application of creams containing antimicrobial ingredients or other antimicrobial fluids beneath the Tegaderm CHG dressing or transparent dressing for skin disinfection, in addition to the requirements of this protocol
EC - 7	The patient is assessed by the investigator as being at high risk of blood stream infection, or known to be sepsis, caused by blood stream infection
EC - 8	The patient has dermatitis, burns, lesions, breaks, eczema, tattoos or other conditions at the catheter insertion site that would interfere with observation in the trial
EC - 9	Women who are pregnant or breastfeeding
EC - 10	Other patients deemed unsuitable for this trial by the investigator's judgment

8.0 INFORMED CONSENT PROCESS

Informed Consent must be obtained for all subjects prior to any study activities being performed or data being collected. The Investigator or designee will review all relevant aspects of the study with the potential study subject that are relevant to the subject's decision to participate throughout the study. The Investigator or designee will provide ample time for

the subject to read and understand the IRB/EC approved Informed Consent Form and to consider participation in the study.

The study subject or legal authorized representative must sign and date the Informed Consent Form. The Investigator or designee must sign and date the Informed Consent Form. The Informed Consent Process must be documented by the Investigator or designee.

The Informed Consent Process includes documentation of the discussion regarding study procedures, subject concerns, that the subject was provided ample time to consider participation, and that all questions were answered prior to participation in any research activity.

The Investigator or designee must file the original Informed Consent Form and provide the subject with a copy of the signed and dated Informed Consent and any other written documentation per local IRB/EC requirements.

In order to minimize pressure and undue influence on vulnerable subjects, the Investigator or designee who is obtaining Informed Consent should ensure appropriate communication techniques, such as visual aids and avoidance of jargon, in order to ensure minimal pressure and undue influence is avoided.

9.0 POINT OF ENROLLMENT AND EXIT

9.1 Point of Enrollment

Following recruitment and eligibility screening, a subject will sign the informed consent form. A subject is considered enrolled in this study at time the Informed Consent process has been completed.

Eligible and consented subjects will be assigned a unique subject identification number, which will not contain information that could identify the subject.

9.2 Point of Exit

Study subjects may exit the study for a variety of reasons. The Investigator shall record the reason for withdrawal and discontinuation of the study in the applicable Case Report Form. These reasons include, but are not limited to:

- Study completion (all study related visit(s) are completed)
- Withdrawal by the Subject
- Withdrawal by Investigator
- Lost to follow-up
- Death
- Study Termination

If a subject withdraws or discontinues participation before study completion, the subject will not be accounted into the per protocol set (PPS) analysis until the required enrollment is reached but will be accounted into the safety set analysis.

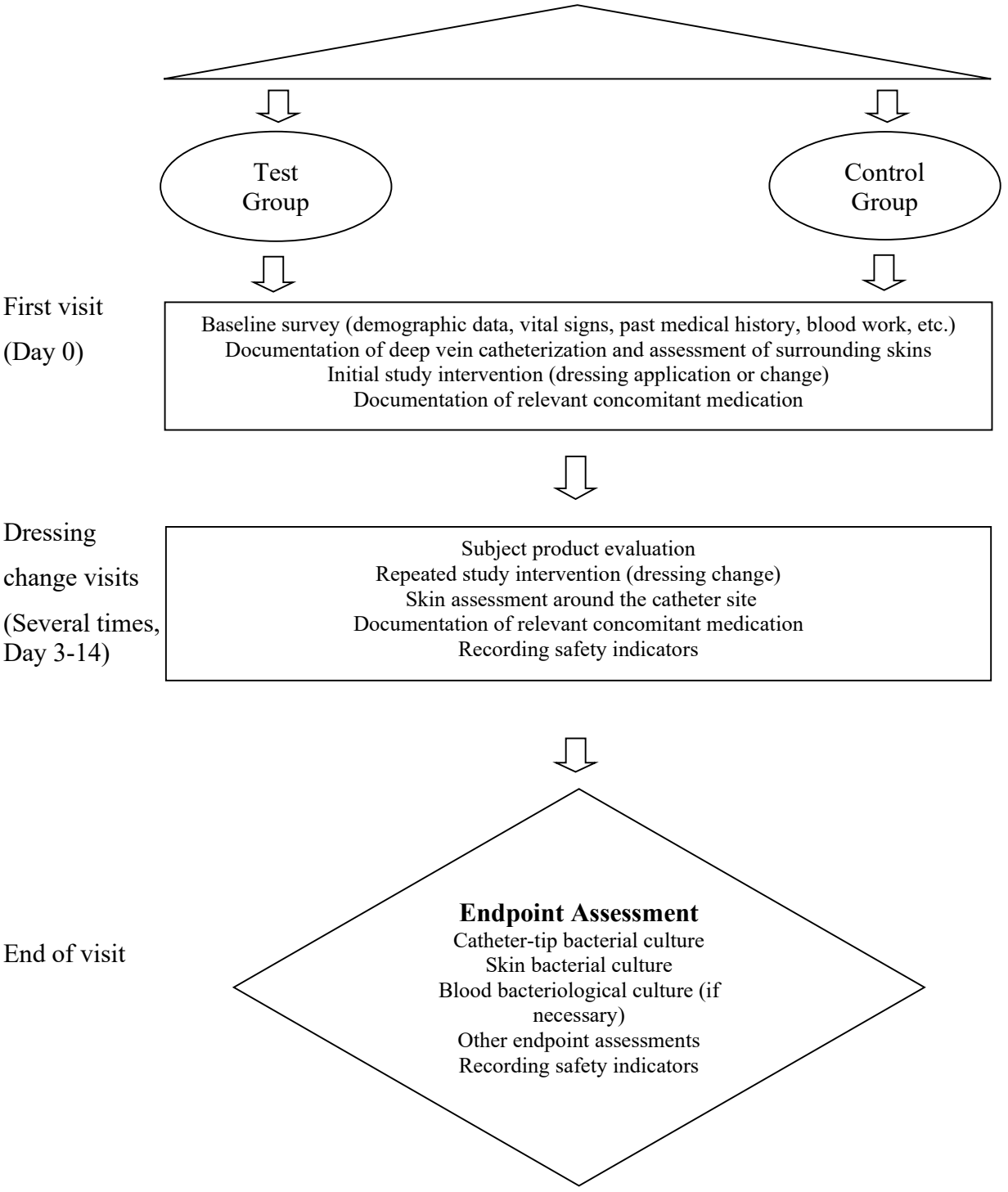
Data collected until the last known contact of study subject may be used in the analysis of study data. Because the subjects in this study are all ICU patients, patients will be considered lost to follow-up if they are transferred out of the ICU or discharged without removal of the CVC. If the study subject withdraws from the study for any reason and there is an ongoing safety event, additional safety event information may need to be collected by the Investigator and shared with Sponsor.

10.0 PROCEDURES

The following sections describe the study procedures and data which will be collected at each procedure for the duration of the study. The data listed below, and any relevant safety data will be collected during this study.

10.1 Procedure Diagram

Signing of informed consent form, enrollment of subjects based on inclusion and exclusion criteria, etc.


Test Group
Control Group
First visit (Day 0)
Baseline survey (demographic data, vital signs, past medical history, blood work, etc.)
Documentation of deep vein catheterization and assessment of surrounding skins
Initial study intervention (dressing application or change)
Documentation of relevant concomitant medication
Dressing change visits (Several times, Day 3-14)
Subject product evaluation
Repeated study intervention (dressing change)
Skin assessment around the catheter site
Documentation of relevant concomitant medication
Recording safety indicators
End of visit
Endpoint Assessment
Catheter-tip bacterial culture
Skin bacterial culture
Blood bacteriological culture (if necessary)
Other endpoint assessments
Recording safety indicators

10.2 Visits

After Informed Consent has been obtained, the following study procedures will be performed. All applicable data are to be recorded in the applicable Case Report Form (CRF).

10.2.1 Randomization

Subjects will be randomly assigned to either the test or control group using an online randomization service by a 1:1 assignment ratio.

10.2.2 Visit 1/Enrollment Visit/Baseline Visit (Study Day 0)

The following procedures will be completed at Visit 1:

1. Confirmation of subjects' eligibility and assessment of inclusion/exclusion criteria;
2. Randomization of patients who met the inclusion criteria;
3. Assessment of the skin condition around the catheter site.
4. Performing immediate dressing changes at all DVC insertion sites based on subjects' conditions at enrollment, using either the subject device 3M™ Tegaderm™ CHG I.V. Securement Dressing or the 3M™ Tegaderm™ Transparent Film Dressing as per randomization results, and following routine departmental nursing procedures;

The following data will be collected at the first visit:

1. Demographic information (height, weight, gender, age at consent);
2. Past medical history and allergic history, collected according to HIS records: Collection of medical and allergic history within the last 3 months related to the inclusion/exclusion criteria, including but not limited to diabetes, immune-related diseases, skin conditions, etc.;
3. Vital signs: Pulse, blood pressure, respiratory rate, body temperature;
4. Relevant laboratory tests, including blood routine examination: Red blood cell (RBC) count, white blood cell (WBC) count, neutrophil ratio, hemoglobin, platelets, C-reactive protein, etc.;

5. DVC type, site of insertion, duration, documentation of any post-puncture exudation, application of any other products such as gauze, hemostatic pads, etc.;

6. Documentation of skin conditions around the catheter site, scoring with reference to the standards for evaluating local skin irritation as listed in the appendix;

7. Medication use in relation to the trial, including mainly fat emulsions, heparin, blood transfusions and antimicrobial drugs;

8. Adverse events, device defects, complaints.

10.2.3 Follow-up visits (number of visits to be marked if there are multiple visits during each dressing change)

Since the expected use duration of the test/control product is a maximum of 7 days, there will be at least one visit on the seventh day into the trial (if catheterization duration is longer than 7 days), and more visits could be taken on a case-by-case basis. The following procedures will be completed at Follow-up visits:

1. Performing dressing changes in accordance with routine departmental nursing procedures;

2. Assessment of skin conditions around the catheter site, with reference to the standards for evaluating local skin irritation as listed in the appendix;

The following data will be collected during the follow-up visit:

1. Date and time of dressing change, site of dressing change, reason for dressing change. Scoring and assessment of edge curling in the case of dressing changes due to severely edge curling in the previous use;

2. Documentation of skin conditions around the catheter site, including erythema, edema, rash, etc., and scoring with reference to the standards for evaluating local skin irritation as listed in the appendix.

3. Any changes in medication use relevant to the trial, including mainly fat emulsions, heparin, blood transfusions and antimicrobial drugs;

4. Adverse events, device defects, complaints.

10.2.4 End-of-treatment Visit

Visit following the completion of dressing securement at the insertion site after removal of DVC. A patient who has multiple catheters withdrawn during the trial should be documented sequentially, but the trial is not to be considered complete at least until the CVC is removed. If replacement of the same type of DVC is performed, only the first removal is recorded and the subsequent replacement is not included in the test or observation.

The following procedures will be completed during the end-of-treatment visit:

1. Assessment of dressing securement performance;
2. Assessment of skin conditions around the catheter site, with reference to the standards for evaluating local skin irritation as listed in the appendix;
3. Photographic documentation of any anomalies;
4. Following departmental routine practice, the tip is cut with sterile scissors after removal, while skin sampling around the insertion site is performed. The samples taken are, under aseptic conditions, sent for pathogenic bacteria testing and species analysis.
5. In case of suspected CLABSI/CRBSI occurrence, sampling and quantitative culture for both catheter and peripheral blood will be performed simultaneously, as well as analysis of pathogenic bacteria species, according to diagnostic evaluation criteria.

The following data will be collected during the end-of-treatment visit:

1. Vital signs: Pulse, blood pressure, respiratory rate, body temperature;
2. Relevant laboratory tests, including blood routine examination: Red blood cell (RBC) count, white blood cell (WBC) count, neutrophil ratio, hemoglobin, platelets, C-reactive protein, etc.;
3. Documentation of dressing securement performance;
4. Documentation of skin conditions around the catheter site, including erythema, edema, rash, etc., and scoring with reference to the standards for evaluating local skin irritation as listed in the appendix.

5. Total duration of DVC placement and duration of application of the test/control dressing;

6. Catheter-tip culture and classification of colonies;

7. Culture and classification of colonies from the skin samples around the insertion site;

8. Any changes in medication use relevant to the trial, including mainly fat emulsions, heparin, blood transfusions and antimicrobial drugs;

9. Confirmation of CLABSI/CRBSI diagnosis;

10. Adverse events, device defects, complaints.

Any Adverse Events, which are not safety related, and which are ongoing at the end of the study, should be marked as 'persistent' per study-specific CRF.

10.3 Schedule of Events

A schedule of events is in the table below:

Table 10.3-1: Schedule

Process	Screening and enrollment Day 0	Dressing change visits	End-of-treatment visit[1]	Withdrawal or discontinuance of visits[2]
Informed consent collection	X			
Assessment of inclusion/exclusion criteria	X			
Randomization	X			
Demographic data [a]	X			
Previous medical history	X			
Vital signs [b]	X		X	X
Routine blood examination [c]	X		X	X
Record of deep vein catheterization	X		X	X
Skin assessment around the catheter site	X	X	X	X
Dressing application or change (multiple times)	X	X		
Documentation of relevant concomitant medication	X	X	X	X
Evaluation of subject product (dressing edge curling, etc.)		X	X	X

Total duration of catheterization			X	
Total duration of test/control dressing use			X	
Catheter-tip bacterial culture			X	
Bacterial culture from skin samples around the insertion site			X	
Blood bacteriological culture			X	
AE/SAE	X	X	X	X
Device defects	X	X	X	X

Note:

a： Date of birth, gender, ethnicity, height, weight, etc.;

b： Pulse, blood pressure, respiration, temperature;

c： Red blood cell (RBC) count, white blood cell (WBC) count, neutrophil ratio, hemoglobin, platelets, C-reactive protein, etc.;

1: There may be multiple visits documented when multiple deep vein catheters are removed in succession;

2. For subjects withdrawing from or discontinuing the trial.

11.0 SAFETY AND EVENT REPORTING

Subject safety and event reporting are important in this study. Investigators are responsible for ensuring that all safety events are recorded in the subject record(s). Events defined in Section 11.3 will be reported to the Sponsor, as applicable, per the timelines in Section 11.4.

11.1 Safety Oversight – Sponsor

Safety oversight will be under the direction of the Medical Director(s) of 3M, which is composed of individuals with the appropriate expertise. The Medical Director(s) routinely review and assess the safety data of the study.

11.2 Safety Recording and Reporting Requirements – Investigator

It is the responsibility of each participating Investigator to ensure all safety events are recorded in the subject's record. The Investigator is responsible for reporting to the Sponsor safety events as defined in Section 11.44.

11.3 Safety and Event Reporting Definitions

This study utilizes the following definitions, as listed in the table below.

Table 11.3-1: Definitions

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device.
Adverse Device Effect (ADE)	An adverse event related to the use of an investigational medical device. This includes any adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device. This includes any event that is a result of a user error or intentional misuse of the investigational device.
Serious Adverse Event (SAE)	Any adverse event that: • Led to death • Led to serious deterioration in the health of the subject, that either resulted in o a life-threatening illness or injury o a permanent impairment of a body structure or a body function o in-patient or prolonged hospitalization, o • medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function • Led to fetal distress, fetal death or a congenital anomaly or birth defect NOTE: Planned hospitalization for a pre-existing condition, or a procedure required by the Clinical Investigation Plan without serious deterioration in health, is not considered a SAE

Term	Definition
Serious Adverse Device Effect (SADE)	An adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event
Unanticipated Serious Adverse Device Effect (USADE)	A serious adverse device effect, which by its nature, incidence, severity, or outcome has not been identified in the current version of the risk analysis report
Device Deficiency (DD)	An inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance, such as malfunctions, use errors, and inadequate labelling
Complaint	Any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a **device** after it is released for distribution

11.3.1 Severity Ratings

The table below defines the severity ratings for events. The Investigator shall ensure rating of reportable events on the applicable Case Report Form.

Table 11.3.1-1: Severity Ratings Definitions

Term	Definition
Mild	An event that is easily tolerated by the subject, causing minimal discomfort and not interfering with everyday activities
Moderate	An event that is sufficiently discomforting to interfere with normal everyday activities
Severe	An event that prevents normal everyday activities

11.3.2 Relatedness

The table below defines the relatedness definitions for events. The Investigator shall ensure rating of reportable events on the applicable Case Report Form.

Table 11.3.2-1: Relatedness Definitions

Term	Definition
Not Related	Relationship to the device or procedure can be excluded
Possible	Relationship with the use of the study device is weak but cannot be ruled out completely.

Causal	The event is associated with the study device or with the procedures beyond a reasonable doubt when:
	- The event is a known side effect of the device
	- The event has a temporal relationship with the study device/application procedures
	- The event involves a body/site or organ that
	  o The device or procedures are applied to;
	  o The device or procedures have an effect on
	- The event follows a known response pattern to the device

11.4 Safety and Event Sponsor Reporting Requirements

This study requires that the following events be reported to the Sponsor, in addition, to completing Case Report Form:

- Reportable Adverse Device Effects, as described in Section 3.3.2
- Any Adverse Events deemed by the Investigator to be related to participation in the study and considered to be due to the study intervention or comparator product.
- All Unanticipated Adverse Device Effects
- All Serious Adverse Events, Serious Adverse Device Effects, Unanticipated Serious Adverse Device Effects
- Device Deficiencies
  Devices meeting the performance expectations but not exceeding performance expectations will NOT be captured as device deficiencies.
- Any Complaint related to any 3M commercially available product used in the study.

The Investigator shall report information relating to the event, and include dates of the event, severity rating, treatment, seriousness and relationship to the investigational device.

Any Adverse Events, which are not safety related, which are ongoing at the end of the study should be marked as "*persistent'* per study specific CRF. Any Events which related to safety OR are persistent and deemed related to the study device, may be followed for an additional 30 calendar days. Events reported by subjects after the last study visit may be reported to the Sponsor up to 30 calendar days from the date of the last visit.

11.4.1 Reporting Timelines

The table below indicates the reporting timelines for events to the Sponsor. The Investigator shall report to local IRB/EC and local regulatory authorities, per local requirements. Reporting to Sponsor begins when study staff are aware of the event. For any event listed in the table below, study Sponsor may request additional information from the Investigator, including but not limited to, medical records, laboratory testing, radiological results, etc. regarding the event.

Table 11.4-1: Safety Reporting Timelines

Type of event	Report to Sponsor	Method
Adverse Events (AE) deemed by the Investigator to be related to participation in the study and considered to be due to the study intervention or comparator product.	Per protocol visits/ Per month	Complete CRF
Unanticipated Adverse Device Effect (UADE)	Per protocol visits/ Per month	Complete CRF
Serious Adverse Event (SAE)/Serious Adverse Device Effect (SADE)	Within 24 hours of study staff becoming aware of event	Initial: Phone/Email to Sponsor Followed by: Complete CRF
Unanticipated Serious Adverse Device Effect (USADE)	Within 24 hours of study staff becoming aware of event	Initial: Phone/Email to Sponsor Followed by: Complete CRF
Device Deficiency (DD)	Within 3 business days of becoming aware of event	Complete CRF

Type of event	Report to Sponsor	Method
Product Complaints on 3M Marketed Product	Within 3 business days of becoming aware of event	Complete CRF

12.0 DEVIATIONS

A deviation is a departure from the Clinical Investigation Plan that will likely affect the safety, rights or welfare of subjects, the scope of the investigation or the scientific quality of the study. A deviation report form shall be completed per event per individual subject. Deviations are documented on a deviation report form or appropriate Case Report Form (CRF). The Investigator is responsible for reporting deviations to the reviewing IRB/EC, per local requirements.

12.1 Deviation Reporting Timelines

Table 12.1-1: Deviation Reporting Timelines

Type of Deviation	Report to Sponsor	Method
Subject safety, rights or welfare; OR Data integrity; OR Compromise the statistical analysis of the study; OR Lack of Informed Consent; OR Inclusion/Exclusion	Within 24 hours of study staff becoming aware of event	Initial: Phone/Email to Sponsor Complete CRF
All other protocol deviations	Per protocol visits	Complete CRF

13.0 PREMATURE STUDY TERMINATION

Both the Sponsor and the Principal Investigator (PI) reserve the right to terminate the clinical investigation at any time. Should this be necessary, the procedures will be arranged on an individual basis after review and consultation by both parties. In terminating the clinical

investigation, the 3M study team and the Principal Investigator will assure that adequate consideration is given to the protection of the subject's interests.

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to study participants, participating Investigators, IRB/EC's and regulatory authorities. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the IRB/EC's, and Sponsor and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Demonstration of efficacy that would warrant stopping
- Insufficient compliance to Clinical Investigation Plan requirements
- Data that are not sufficiently complete and/or evaluable
- Determination that the primary endpoint has been met
- Determination of futility

Suspended studies may resume once concerns about safety, Clinical Investigation Plan compliance, and data quality are addressed, and satisfy the Sponsor, IRB/EC and regulatory authorities.

14.0 MONITORING

Study monitoring is conducted to ensure that the rights, safety and well-being of study participants are protected, that the reported study data are accurate, complete, and verifiable, and that the conduct of the study is in compliance with the currently approved Clinical Investigation Plan (CIP), with GCP, and with applicable regulatory requirement(s).

3M or its designee, as Sponsor of this clinical investigation, is responsible for ensuring the proper conduct of the clinical investigation with regard to CIP adherence and validity of the data recorded on the CRFs. 3M, has therefore assigned study monitor(s) to this clinical investigation. The progress of the clinical investigation will be monitored by:

- Periodic and/or remote review
- Telephone communications
- Review of CRFs and source documents (e.g. subject records)

The study monitor(s), other authorized representatives of the Sponsor, representatives of the IRB/EC, or regulatory authorities may inspect all documents and records required to be maintained by the Investigator, including but not limited to, subject records (office, clinic, or hospital) for the participants in this study. The clinical study site will permit access to such records. The Investigator will give 3M study monitor(s) direct access to source documents that support data on the CRFs. This includes any electronic records.

Investigator non-compliance of required study responsibilities will require Sponsor sanctions to alleviate the non-compliance. Including corrective and preventative actions up to and including disqualification.

Details of clinical site monitoring are documented in a Monitoring Plan (MP). The MP describes in detail who will conduct the monitoring, at what frequency monitoring will be done, at what level of detail monitoring will be performed, and the distribution of monitoring reports.

Independent audits may be conducted by GCP ClinPlus Co., Ltd, CHINA to ensure monitoring practices are performed consistently across all participating sites and that monitors are following the MP.

15.0 ROLE OF SPONSOR REPRESENTATIVE

In addition to study monitoring, the Sponsor, or their representatives may conduct the following tasks during this study:

- Audits of the Investigator
- Provision of technical support/product specific training for the study device

16.0 DEVICE ACCOUNTABILITY

The device(s) under investigation will not be distributed to the investigational site until all agreements between the site and 3M are finalized and IRB/EC approval has been obtained.

3M requires that Investigators maintain device accountability and security of the devices at all times. The Investigator or designee will:

- Maintain and account for devices at the Investigator site
- Keep devices in a secure storage area, accessible only to authorized individuals.
- Dispense devices only to subjects properly enrolled in and eligible for the study.
- Return all unused investigational materials to the Sponsor at the end of the study or dispose of as agreed upon.

16.1 Device Labeling

Devices utilized in this study will be labelled according to applicable regulations. A sample label will be retained in the Investigator Site File.

16.2 Additional Study-Specific Equipment/Device(s)

Additional study-specific equipment/devices used in this study shall be maintained, calibrated (if applicable) and ensured to be functioning correctly during the study, in accordance with this study Clinical Investigation Plan or applicable site policy and regulatory requirements. The Sponsor should be notified of any anticipated or known issues with the device functionality that may impact the study conduct or outcome.

17.0 CONFIDENTIALITY

Participant confidentiality and privacy is strictly held in trust by the participating Investigators, their staff, and the Sponsor(s) and their authorized representatives. This confidentiality is extended to cover testing of biological samples and genetic tests in addition to the clinical information relating to participants. Therefore, the Clinical Investigation Plan, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study, or the data will be released to any unauthorized third party without prior written approval of the Sponsor. All research activities will be conducted in as private a setting as possible.

Study data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at 3M or approved supplier. This will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The electronic data capture system used by clinical sites and by 3M research staff will be secured and password protected. At the end of the study, all study databases will be de-identified and archived at 3M or approved supplier.

17.1 Future Use of Stored Collected Specimens

With the participant's approval and as approved by the local IRB/EC, de-identified biological samples will be stored at 3M with the same goal as the sharing of data with the 3M researchers.

During the conduct of the study, an individual participant can choose to withdraw consent to have biological specimens stored for future research. However, withdrawal of consent with regard to biosample storage may not be possible after the study is completed.

18.0 DATA HANDLING AND RECORD KEEPING

Data collected for this study will be analyzed and stored at 3M or an approved supplier for use by researchers including those outside of the study. Permission to transmit, store and use data outside of the study will be included in the informed consent.

18.1 Data Collection and Management Responsibilities

Data collection is the responsibility of the clinical study staff at the site under the supervision of the site Investigator. The Investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents should be completed in a neat, legible, permanent and un-editable manner to ensure accurate interpretation of data. Data recorded in the electronic case report form (eCRF) derived from source documents must be consistent with the data recorded on the source documents.

Data (including adverse events (AEs), concomitant medications, and expected adverse event data) will be entered into a 21 CFR Part 11-compliant data capture system provided by 3M. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate.

18.2 Study Records Retention

The study participant's information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB/EC, Institutional policies, regulatory authorities or Sponsor requirements.

No records will be destroyed without the written consent of the Sponsor. It is the responsibility of the Sponsor to inform the Investigator when these documents no longer need to be retained.

18.3 Sponsor Oversight

Routine review of submitted study information by the Sponsor will be conducted to ensure Clinical Investigation Plan compliance. Items reviewed include but are not limited to: adverse events, deviations, number of withdrawn/terminated subjects; which all may impact the completion of the study. Appropriate measures may be taken to ensure Investigator compliance with the Clinical Investigation Plan.

19.0 STATISTICAL CONSIDERATIONS

This is a prospective, randomized, open-label, parallel-group controlled, single-center study designed to explore whether the subject product effectively reduces bacterial colonization in comparison with the control product. Subjects will be divided into two groups based on the random number table.

For continuous data, descriptive statistics will include the number of subjects, mean, standard deviation, median, minimum and maximum values. For categorical data, descriptive summaries will be made by frequency and percentage. Unless otherwise specified, a two-sided test will be used for all statistical tests, and a p-value of less than 0.05 will be considered statistically significant for the difference being tested.

19.1 Statistical Hypotheses

19.2 Sample Size Determination

This study will use a positive two-sided Z test for continuity calibration and use the O'Brien-Fleming expenditure function to determine the test boundary. Assuming a baseline value of 18.7% for CVC tips colonization rate in the control group (this figure is reported by a domestic epidemiological survey) and a reduction rate of 50.0%, each group should contain at least 220 patients with CVC to reach 80% likelihood at 5% significance level. A total of 440 valid cases are required in both groups combined. An interim analysis is scheduled for this study and will be conducted after completion of follow-up visits of 220 subjects to correct for the pre-defined sample size.

19.3 Population for Analyses

Full analysis set (FAS): The set of subjects determined according to the principle of Intention to Treat (ITT) refers to the data set composed by all subjects who are involved in the trial randomly and have used the trial product. The missing data were carried forward using the strategy of WCCF (Worst Case Care Forward) in case the primary efficacy endpoints of the patients were not observed. FAS is the primary analytical data set for evaluating validity.

Per protocol set (PPS): PPS is a subset of the FAS and includes subjects randomly assigned to treatment with a test or control device who have not experienced significant protocol deviations. The PPS is the secondary analytical data set for evaluating validity.

Safety analysis set (SS): This includes all subjects who have been formally enrolled and completed catheterization and dressing securement with the catheter in place for more than 24 hours. This data set is used to evaluate the safety of this trial.

19.4 Statistical Analyses

For patient baseline characteristics and demographic data, quantitative data will be analyzed based on t-test or rank sum test, and qualitative information will be analyzed based on Chi-square test or Fisher's exact test. CVC tip bacterial colonization rates, PICCO/hemodialysis catheter bacterial colonization rates, catheter-related bloodstream infection rates, and microbial species analysis will be analyzed by chi-square test or Fisher's exact test. Other results collected in this study, such as wearing duration, frequency of replacement, skin condition, and number of deaths, will be analyzed using t-tests or rank sum tests accordingly. The O'Brien-Fleming expenditure function will be used twice in succession to determine the test boundaries.

In addition, descriptive summaries of effectiveness and safety evaluation indicators will be presented for the entire trial and for subjects in each group. For continuous data, the data will be summarized by number of subjects, mean, standard deviation (SD), median, minimum and maximum values. For categorical data, they will be summarized by frequency and corresponding percentage.

19.5 Planned Interim Analyses and Criteria for Clinical Investigation

Interim analysis will be conducted at enrollment to 220 subjects, and the total CVC tip colonization rate obtained from the interim analysis will be used to recalculate and evaluate the sample size.

19.6 Procedures for Missing, Unused or Spurious Data

Data for the validity evaluation indicator and safety evaluation indicator will not be interpolated. The interpolation of incomplete data will be further described in SAP.

Unused or erroneous data in the database will be identified and processed during the data management process.

19.7 Procedures for Reporting Deviations from Statistical Plan

If the method of analysis in this protocol changes before the data is locked, it will be documented in SAP. If there are changes to the analyses in the final SAP after data locking, they should be documented in the Statistical Analysis Report (SAR) and the Clinical Study Report (CSR).

19.8 Validation Plan

Independent validation of statistical plans and outputs will not be performed, and standard validation methods should be used (self-review of codes and logs, consistency review with other data sets and within the report, etc.).

20.0 CONFLICT OF INTEREST

The independence of this study from any actual or perceived influence, such as by the medical device industry, is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial. The Sponsor has established procedures for all Investigators to

disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

21.0 CLINICAL INVESTIGATION PLAN MODIFICATIONS

Modifications to this CIP may be necessary to protect the safety of the subjects and integrity of the data. In collaboration with the Investigator(s), modifications will be documented and submitted for ethical and regulatory approval (as required) prior to implementation. All changes will be evaluated for impact per Sponsor standard operating procedures (SOPs). Modifications will be considered implemented after all ethical and regulatory approvals (as required) are received and all key Sponsor and site staff has been trained.

22.0 PERIODIC REVIEWS

Ongoing reviews by IRB/EC are required for the duration of the clinical study. The Investigator will comply with local IRB/EC requirements for ongoing reviews, at a minimum annually. The Sponsor will provide an annual study report to participating Investigators.

23.0 INSURANCE

The Sponsor shall provide clinical study related insurance covering the reasonable, and necessary costs of diagnostic, therapeutic and medical treatment including hospitalization costs (treatment costs) for such participant injuries following the administration or use of the study device(s) in accordance with this clinical investigational plan and in accordance with the national regulations. The Sponsor may reimburse the institution and/or study participants for treatment costs depending on who incurred such treatment costs. The Sponsor will not be responsible for paying for or reimbursing treatment costs if (i) the injury is attributable to the negligence or misconduct of any agent or employee of the institution or Investigator, or the failure of such persons to comply with a study protocol, (ii) the treatment costs are covered by the study participant's medical or hospital insurance coverage, or (iii) the treatment costs arose as a result of the treatment of normal progression of the study participant's disease or

injuries resulting from interventions that the study participants would have incurred had they not participated in the study.

24.0 PUBLIC REGISTRATION AND PUBLICATION

The Sponsor shall ensure that this study will comply with any required national registration requirements. This study will be conducted in accordance with the applicable publication and data sharing policies and regulations.

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26.0 GLOSSARY

Abbreviations	Definitions
ADE	Adverse Device Effect
AE	Adverse Events
CHG	Chlorhexidine Gluconate
CLABSI	Central Line Associated Bloodstream Infections
CRA	Clinical Research Associate
CRO	Contract Research Organization
CRBSI	Catheter Related Blood Stream Infections
CVC	Central Venous Catheter
DVC	Deep Venous Catheters
eCRF	electronic Case Report Form
EC	Ethics Committee
EDC	Electronic Data Capture
FAS	Full Analysis Set
FDA	Food and Drug Administration
GCP	Good Clinical Practice
ICF	Informed Consent Form
IFU	Instruction for Use
NMPA	National Medical Products Administration
PD	Protocol Deviation
PI	Principal Investigator
PICCO	Pulse Index Continuous Cardiac Output

PPS	Per Protocol Set
RBC	Red Blood Cell
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Events
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SD	Standard Deviation
SMV	Site Monitoring Visit
SOP	Standard Operating Procedure
SS	Safety Analysis Set
WBC	White Blood Cell

27.0 STUDY-SPECIFIC APPENDICES

Appendix A

REVISION HISTORY

The purpose of this appendix is to describe modifications made to this document, in detail, when moving from Version 1.0 to Version 2.0.

Overall summary of changes		
Version 2.0: Exclusion Criteria EC-3 and EC-7		
Section modified	**Original text**	**Updated text**
1.0 Synopsis- Selection of Subjects-EC-3 7.2-1 Exclusion Criteria EC-3	The patient is assessed by the investigator as being at high risk of infection, or known to be immune-deficient, based on the environment, duration and site conditions of catheterization.	The patient is assessed by the investigator as being at high risk of CLABSI, or known to be CLABSI, based on the environment, duration, and site conditions of catheterization.
1.0 Synopsis- Selection of Subjects-EC-7 7.2-1 Exclusion Criteria EC-7	The patient is clinically diagnosed with sepsis or bacteremia.	The patient is assessed by the investigator as being at high risk of blood stream infection, or known to be sepsis, caused by blood stream infection.

Appendix B

Evaluation Criteria

CLABSI/CRBSI evaluation criteria

CLABSIs: Primary bloodstream infections in hospitalized patients occur during the use or within 48 hours after removal of indwelling central venous catheters and are unrelated to the presence of infections at other sites. CRBSI: Catheter-induced bloodstream infections are primary infections that occur in patients with a central venous catheter and where there is laboratory evidence that the catheter is the source of the bloodstream infection.

Patients who develop infection symptoms such as fever, chills, and/or hypotension after catheterization and at least one peripheral venous blood culture positive of bacteremia or fungemia without any other obvious sources of bloodstream infection show one of the following: semi-quantitative catheter-tip culture ≥15 cfu, while the same microorganism (species) is isolated from both the catheter-tip culture and the peripheral blood culture; the ratio of bacterial growth (cfu/ml) between quantitative catheter-tip and peripheral blood cultures, which are performed concurrently, is greater than 3:1; the positive alarm time of the blood specimen is more than 2 hours earlier than that of the peripheral equivalent specimen.

Diagnostic criteria

a. Retain the catheter:

If two sets of blood cultures are positive and present the same species

- In the absence of evidence of other infections, it indicates possible CRBSI;
- If the same pathogen is found in both sets of cultures and the blood culture from the catheter reports positive 120 minutes earlier than the one from the peripheral vein: It indicates CRBSI if there is no evidence of other infections (it may also indicate CRBSI if the difference in time to positivity between the two sets of blood cultures is less than 120 minutes but have the same identification and drug sensitivity results).
- If both sets of blood cultures are positive, and the bacterial count from catheter blood cultures is at least five times higher than that of peripheral venous blood cultures,

it indicates possible CRBSI (for manual quantitative blood culture systems) if there is no evidence of other infections.

If only the catheter blood culture tests positive: It will not be a conclusive evidence of CRBSI, but may be due to bacterial colonization or contamination during blood specimen collection.

If only the peripheral venous blood culture tests positive: It will not be a conclusive evidence of CRBSI; however, if it is Staphylococcus aureus or Candida, in the absence of other evidence of infection, it indicates possible CRBSI.

If both sets of blood cultures are negative: It indicates no CRBSI.

The reference table is as follows:

Catheter	Peripheral vein	Conditions	Judgment of results
+	+		Possible CRBSI
+	+	The catheter-tip culture reports positive 120 minutes earlier than the peripheral vein culture	Indicating CRBSI
		Catheter bacterial concentration is 5 times higher than peripheral vein	
+	-		Cannot be determined
-	+		Cannot be determined
		In the case of Staphylococcus aureus, or Candida	Indicating CRBSI
-	-		Not CRBSI

b. Removal of catheters:

If one or more sets of blood cultures are positive and the catheter-tip culture is positive: The detection and drug-sensitivity spectrum analysis indicate the same species in both types of cultures: It indicates possible CRBSI;

If one or more sets of blood cultures are positive and the catheter-tip culture is negative: If the cultures are positive for Staphylococcus aureus or Candida and there is no evidence of other infections, it indicates possible CRBSI and may require additional positive blood cultures of the same organism to reach a conclusion;

If the blood culture is negative and the catheter-tip culture is positive: It indicates catheter colonization, not CRBSI;

If both sets of blood cultures and end-of-catheter cultures are negative: It indicates no CRBSI.

The reference table is as follows:

Catheter tip	Peripheral vein 1	Peripheral vein 2	Judgment of results
+	+	+	Possible CRBSI
+	+	-	
-	+	-	Cultures are positive for Staphylococcus aureus or Candida and there is no evidence of other infections, it indicates possible CRBSI
-	+	+	
+	-	-	Catheter-colonizing bacteria
-	-	-	Not CRBSI

Lift Scale

Score	Description of Sample Lift
0	No lift
1	1 - 25%
2	26 - 50%
3	51 - 75%
4	76 - 99%

5	Missing

Skin Irritation Scale- Erythema

Score	Description of Response
0	No Erythema
1	Very slight erythema (barely perceptible- edges not well defined)
2	Well-defined erythema (pale red in color and area definable)
3	Moderate erythema (definite red in color and rea definable)
4	Severe erythema (beet or crimson in color)

Skin Irritation Scale- Edema

Score	Description of Response
0	No Edema
1	Very slight edema (barely perceptible edges not well defined)
2	Well-defined edema (area definable but not raised more than 1 mm)
3	Moderate edema (area well definable and raised approximately 1 mm)
4	Severe edema (area raised more than 1 mm and extending beyond exposure area)

Itch

Score	Description of Response
0	No itching
1	Slight itching
2	Moderate itching
3	Extreme itching: could not stop scratching at any time/ need a treatment