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Clinical Study Protocol

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E6 Good Clinical Practice:
Consolidated Guidance

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

Clinical Study Protocol

Study Number and Protocol Title	*Study EM-05-014222: National, cross-sectional, multicenter study to estimate the point prevalence of **p**eripheral **i**ntravenous catheter-related complication**s** in Brazil: a quality improvement study* **(PIVS)**
Sponsor	**3M do Brasil Ltda.** Rod. Anhanguera, s/n km 110 CEP (Zip Code): 13181-900 Sumaré-SP, Brasil
3M Study Monitor	[redacted]
3M Advisor	[redacted]
3M Medical Monitor	[redacted]

Approver List (3M Approvers Only):

Signer	Role	Date Signed
[redacted]		

cc: Clinical Study Folder
Investigator Study Documentation File (Regulatory Binder)

3M Study Number: EM-05-014222

Protocol Title: *National, cross-sectional, multicenter study to estimate the point prevalence of peripheral intravenous catheter-related complications in Brazil: a quality improvement study (PIVS)*

Investigator Agreement: I have read the protocol referenced above and I agree to conduct the study in accordance with the ethical principles that have their origin in the Declaration of Helsinki, Good Clinical Practice (GCP) and applicable state and federal regulations.

Investigator Name: _____

Signature/Date: _____
Signature Date

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1. Background Information

1.1 Introduction

Hospital personnel continually survey the infectious and mechanical complication rates related to short-term Central Venous Access Devices (CVADs). Routine reporting to hospital administration and/or government agencies has become mandatory in many countries, since these CVAD complications can significantly impact patient outcomes and healthcare costs. However, routine or mandatory surveillance (audits) of short peripheral IV catheter (PIVC) therapy does not occur in hospitals globally, despite the recognized impact of PIVC failure. PIVC failure is defined as any premature removal of an PIVC before the end of treatment, other than for routine replacement (includes phlebitis, infiltration, occlusion, accidental removal, leaking, dislodgement and local or catheter-related bloodstream infection[2,12]).

PIVC therapy is beneficial to patients requiring medications or fluids that can be administered using peripheral veins and these catheters: (1) are used considerably more often than the CVADs, (2) have an overall failure rate that lies between 35% and 50%[2, 3, 4, 5] and (3) can lead to bloodstream infections, which are less frequent than those associated with CVADs but are still serious complications[6]. Moreover, the rates of these and other complications that are known to contribute to PIVC failure, such as phlebitis and infiltration, are under-reported[8]. Understanding the impact of PIVC-related complications is paramount, given that PIVC failures can lead to delays in IV therapy, increased length of hospital stays and higher hospitalization costs[7].

According to Alexandrou *et al*. (2015)[8], there are currently little data on PIVC management practices across different regions of the world, making it difficult to identify contributing factors for PIVC failure in general and for PIVC-related complications in particular. One of the main issues arising as a consequence of inadequate PIVC management practices is catheter dislodgment. Patients having securement-related issues, which might be associated with poor dressing and/or securement devices, are at greater risk for infection, thrombus formation and air embolism and are likely candidates for catheter replacement.

Therefore, though evidence-based strategies have been developed to reduce PIVC-related complications, it is not known whether these strategies are consistently applied in the acute care setting[6]. Audits and benchmarking of practice are necessary to drive improvement strategies and incite the development of interventional studies.

A prevalence study is a quick method to audit and measure PIVC-related complications and compliance to evidence-based strategies. The Infusion Therapy Standards of Practice (2016) recommend regular evaluations of adverse events associated with PIVC use, such as infiltration, phlebitis, and/or bloodstream infection in populations of interest. Incidence studies, point prevalence studies and analyses of International Classification of Diseases (ICD) codes documented in electronic medical records are types of studies that can be used to meet this purpose. These regular evaluations must: (1) use consistent definitions; (2) compare current failure rates to internal historical data, to identify areas of improvement; and (3) result in data that are provided to the institution's leadership.

In this national, multicenter, cross-sectional study, healthcare professionals working in acute care hospitals, with expertise in PIVC therapy, will audit patient medical records and directly observe PIVC insertion sites on select hospital wards. The prevalence of PIVC-related complications that are identified upon observation will be determined. Furthermore, a

summary of PIVC management practices at each participating hospital or ward will be obtained.

1.2 Risk/Benefit Summary

Risks to implementing this study are minimal. It is an observational study, centered on the study of PIVCs indwelling in adult patients admitted in acute care hospitals in Brazil, but not on the patients themselves.

Products used in PIVC therapy have some benefit in maintaining the PIVC's location and patency while the needed medical therapy is infused via the catheter. Yet, these benefits are sometimes overshadowed by several potential risks. The risks of implementing PIVC therapy include, but are not limited to: phlebitis, infiltration, extravasation, skin injury, ecchymosis or hematomas, local infection at the insertion site, catheter-related blood stream infections (CRBSI), catheter dislodgement, deep venous thrombosis, excessive blood loss from a disconnected infusion system, among others.[10,11]

These risks or complications might be influenced by: (1) the adhesive and catheter stabilizing properties of the dressing cover and/or tape; (2) the ability of the nurse to visualize the site for early detection of complications; (3) the effectiveness and duration of the skin's antimicrobial preparation; (4) the aseptic insertion technique and site location of the PIVC; (5) the design and gauge of the PIVC; (6) the medicinal or fluid therapy infused through the catheter; and (7) patient-related factors, e.g. gender, activity, skin condition, co-morbidities and history of previous PIVC complications. [4,7,10,11]

When products for PIVC therapy are effective, properly used and accompanied by good clinical practice, the benefits of PIVC therapy will significantly outweigh the risks identified above. The products that will be under observation during this study are all approved by the Brazilian regulatory agencies and are currently used at the hospitals for PIVC therapy. If the products are used as intended, the benefit obtained with the use of these medical devices should outweigh the risks associated with each one.

It is expected that the prevalence study data will contribute to the site's quality improvement program and help drive the nurses to: (1) evaluate and procure products to reduce complications; (2) develop and implement training programs on evidence-based strategies and (3) continue a surveillance practice to determine if new or modified interventions for PIVC management impact patient outcomes over time[7]. Furthermore, this study can provide a foundation for a wider point prevalence study of PIVC-related complications in Brazil and/or to design and implement further clinical studies of PIVC management.

The Sponsor plans to use the data (de-identified) of this study for the pre-interventional phase of a pre-post interventional study. The data are to be compared to prevalence data obtained after the introduction of a dressing, which would comprise the post-interventional phase of the abovementioned pre-post interventional study.

All necessary measures will be implemented to ensure the confidentiality of the research participants' data. However, a minimal risk of data confidentiality breaches cannot be entirely ruled out.

1.3 Investigational Material Application

No investigational materials will be provided or used in this prevalence study. All PIVC-related products used at or on the PIVC insertion sites by the participating hospitals are approved by the Brazilian regulatory agencies, routinely purchased by the hospital and available to the physicians and nurses at the time of the study. Characteristics of the products

used at the PIVC insertion sites observed during the study will be documented. All PIVC brands will be observed in the context of this study.

1.4 GCP and Regulatory Requirements

The whole conduction of the study will be performed in compliance with the protocol, the principles laid down on the Declaration of Helsinki, ICH's Good Clinical Practice (GCP) and all applicable regulatory requirements.

This research project was prepared in accordance with Resolution No. 466 of December 12, 2012 of the National Health Council, which establishes the ethical standards for research involving human beings. Data collection will occur only after approval of the study and its documents by the Ethics Committee of each research center.

1.5 Study Population

All persons with 18 or more years of age, admitted to the participating facility and who meet the eligibility criteria in Section 4.

2. Study Objectives and Purpose

2.1 Primary Objective

- To determine the prevalence of any PIVC-related complications, clinical **or** mechanical, in acute care hospitals in Brazil.

2.2 Secondary Objectives

- To determine the prevalence of simultaneous clinical **and** mechanical PIVC-related complications in acute care hospitals in Brazil.
- To determine the prevalence of PIVC-related clinical complications, overall and by type, in acute care hospitals in Brazil.
- To determine the prevalence of PIVC-related mechanical complications, overall and by type, in acute care hospitals in Brazil.
- To determine the prevalence of PIVC-related quality issues, overall and by type, in acute care hospitals in Brazil.
- To describe the standards of practice for PIVC management employed in acute care hospitals in Brazil.

2.3 Exploratory Objectives

- To explore the association between PIVC-related complications and subjects' socio-demographic characteristics, and other baseline characteristics.

3. Study Design

3.1 Study Type

This will be a national, multicenter, cross-sectional study to assess the prevalence of PIVC-related complications in Brazil. Estimates of the prevalence of clinical and mechanical complications, as well as quality issues associated with PIVC management, will be studied. Moreover, hospital- or ward-specific standards of practice for PIVC management will be described. The study will be considered the pre-study stage of a pre-post interventional study. The de-identified data from this study will be used to calculate the effect of the intervention on the PIVC complication rate.

3.2 Study Setting

The study is expected to be conducted at three acute care centers located in Brazil. Assessment of PIVCs insertion sites and related complications, as well as of standards of practice for PVIC management, will take place at the hospitals' general or specialty admission wards. Wards where the study procedures are not to be carried out include outpatient clinics, mental health wards, emergency wards and burn units.

3.3 Study Procedures

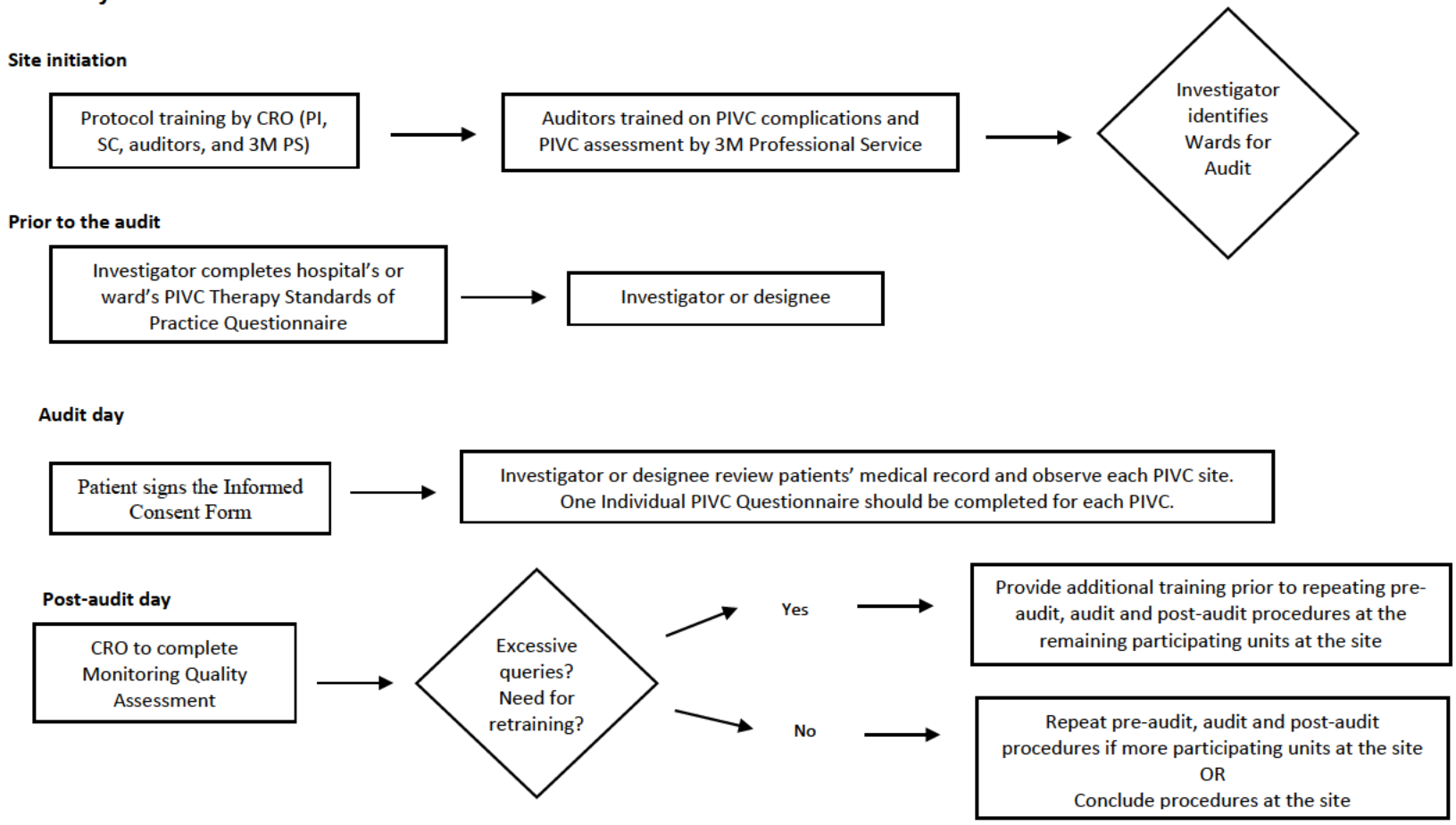

Figure 1– Flowchart of study activities

All of the study team will receive training on the study protocol and other protocol-related procedures prior to study start. At each center, the study will only start after the study protocol and PIVC site assessment training is completed (Figure 1).

Study procedures will be completed in a single center (pilot study site) prior to initiating study activities in the remaining centers. This strategy will allow for the adjustment of any training or monitoring needs identified at the first center. At each study site, including the pilot study site, study activities at the participating wards will be performed in parallel. The Principal Investigator (PI) will be responsible for selecting, at each site:

- The wards that will be audited within the context of this study.
- The healthcare professionals (auditors) that will be responsible for auditing the participating wards. Auditors will be healthcare professionals (e.g. nurse, resident physicians) with extensive experience in PIVC therapy and who are employed by the study site.

Once the PI has selected the hospital's wards that will be participating in the study, the PIVC Therapy Standards of Practice Questionnaire will be completed by him/her or a designee. If there are individual PIVC therapy standards of practice per ward, rather than hospital-wide standards, the PI will interview the ward nurse manager or a ward clinician of the selected wards and complete the PIVC Therapy Standards of Practice Questionnaire for each ward.

To minimize subject selection bias, all subjects will be identified and invited to participate in the study consecutively, as the auditor goes through the ward. An informed consent process will be carried out by the PI, auditor or a designee. After the subject provides his/her written informed consent to participate in the study , data will be collected from the subject's medical records and by observation of the PIVC site. All PIVC sites, regardless of catheter commercial brand, should be assessed. Data on each PIVC site will be recorded on the Individual PIVC Questionnaire.

In addition to collecting general characterization data on the patient and the PIVC, the auditor will be observing the PIVC site for presence of the following complications (see Appendix I for definitions):

- Clinical complications:
  - Phlebitis:
    - According to grade: grade 1-4
    - According to etiology: mechanical, chemical, infective
  - Hematoma
  - Ecchymosis
  - Skin injury
  - Local infection
- Mechanical complications:
  - Catheter dislodgement
  - Occlusion
  - Extravasation
  - Infiltration (grade 1-4)
  - Leaking at the insertion site

The PIVC will also be evaluated for the presence of the following quality issues:

- Unstable PIVC
- Blood reflux
- Uncontrolled IV infusion rate
- Site dressing partially detached
- Site dressing totally detached (site exposed to environment)

- Medical tape added to dressing edges
- Unclean dressing
- Discomfort at site with or without palpation
- Uncovered tubing access port
- Lack of visibility at the PIVC site

If the patient has more than one PIVC, one questionnaire will be completed for each PIVC.

Once the wards' audits are concluded, the study-specific electronic case report forms (eCRFs) will be completed by the PI or study designee. The sponsor or sponsor's representative will perform the monitoring activities and, based on the number or type of inconsistencies/ queries raised, the monitor may deem that the site requires additional training. Once the additional training is complete, the audit process will continue with any changes deemed necessary by the monitor to improve the quality and quantity of data collected.

The process of PIVC-related data collection will be repeated at each study site until at least 100 PIVCs have been audited (Table 1).

Table 1 - Study data collection and procedures per audited ward

Study procedures[a]	Pre-audit	Audit day
Completion of hospital's or ward's current PIVC Therapy Standards of Practice Questionnaire[b]	X	
Inclusion and exclusion criteria review		X
Informed consent form signature		X
Completion of Individual PIVC Questionnaires		X

a. Procedures and timeline to be repeated if more than one ward is to be audited at the study site.
b. Repeat survey of current PIVC standards of practice, if the standards are ward-specific.

3.4 Study Data Sources

Information on the hospital's or ward's standards of practice for PIVC management will be recorded by the PI or designee into the Hospital/Ward PIVC Therapy Standards of Practice Questionnaire.

After the subject provides his/her written informed consent, subject and PIVC-related data will be collected from the subject's medical records and by observation of the PIVC insertion site. This information will be recorded into the Individual PIVC Questionnaire.

The investigator will be responsible for ensuring that all the required data is collected in the study-specific eCRF. No subject identifiable information will be captured.

3.4.1 Study Variables

The following variables will be collected in this study:

- Hospital/Ward standards of practice for PIVC management:
  - Existence of standards of practice for PIVC management at the hospital or ward: yes/no

- Skin antiseptic solution used prior to PIVC insertion:
  - Sterile or nonsterile normal saline
  - Isopropyl alcohol (and percent alcohol concentration)
  - Ethanol alcohol (and percent alcohol concentration)
  - Povidone iodine (and percent concentration)
  - Chlorhexidine gluconate (CHG) in alcohol (and percent CHG concentration)
  - CHG alone
  - Other (specify)
  - Not defined

- Skin antiseptic container:
  - Multi-use bottle
  - Single-use sterile container
  - Not defined

- Skin antiseptic solution applicator:
  - Non-sterile gauze or absorbent pad
  - Non-sterile cotton ball
  - Sterile gauze or absorbent pad
  - Sterile cotton ball
  - Swab sticks
  - Wipes or Wipettes
  - Other (specify)
  - Not defined

- Frequency of PIVC site rotation:
  - Every 72 hours
  - Every 96 hours
  - As clinically indicated
  - Other (specify)
  - Not defined

- Frequency of PIVC assessment:
  - Every 4 hours
  - Every 8 hours
  - Every 24 others
  - Other (specify)
  - Not defined

- Method used to access or connect the catheter or primary IV tubing:
  - Needle-based system
  - Needleless-based system
  - Access extension (side injector)
  - 3-way open female luer
  - Not defined

- Use of disinfectant cap to cover access ports, needleless caps or hubs when not in use or not connected to another IV set: yes, sometimes, no

- Cap used to protect and seal the access ports or catheter hub when no infusion is administered:

        - Caps that accompany the IV tubing
        - Needleless cap only
        - Disinfection cap (Curos, SwabCap, other (specify))
        - Caps from a syringe needle
        - No cap, end is directly connected to other tubing
        - Access port not covered
        - Not defined

    - Solution used to disinfect the access ports of the IV bag/bottle, catheter and tubing prior to attachment:
        - 70% isopropyl alcohol
        - 70% ethanol alcohol
        - CHG solution (and percent CHG concentration)
        - Other (specify)
        - Not defined

    - Technique used to disinfect the access ports:
        - Single swipe
        - Twisting motion (timed or not)
        - Back and forth motion with friction (timed or not)
        - Other (specify)
        - Not defined

    - Patients who receive infusion therapy through an infusion pump:
        - All patients receiving IV medication, electrolyte or solution
        - ICU patients only
        - Limited to patients receiving specific medications
        - None of the patients
        - Other (specify)
        - Not defined

    - Responsible person who adds medications and electrolytes to IV infusion bottles or bags:
        - Nurse
        - Pharmacist
        - Physician
        - Nurse technician
        - Other (specify)
        - Not defined

    - Environment where medications and electrolytes are added to IV infusion bottles or bags:
        - Nurses' station
        - Medication room
        - Patient's room/ward
        - Pharmacy
        - Not defined

- Socio-demographic variables:
    - Date of birth
    - Initials
    - Gender

- Individual PIVC variables:
  - Date and time of PIVC audit
  - Date and time of PIVC insertion
  - Responsibility for PIVC insertion:
    - Nurse
    - Physician
    - Nurse technician
    - Other (specify)
    - Unknown/Not documented
  - Department where PIVC was inserted:
    - Emergency department
    - Operating room
    - Intensive or Critical Care Unit (ICU)
    - General ward/clinic
    - Radiology or other procedure room
    - Ambulance/Emergency Medical System (EMS)
    - Other hospital
    - Unknown/Not documented
  - PIVC location:
    - Left or right hand
    - Left or right wrist
    - Left or right forearm
    - Left or right antecubital fossa
    - Left or right upper arm
    - Left or right foot
    - Left or right side of the head
    - Other (specify)
  - Reason for PIVC insertion:
    - IV fluids
    - IV medications
    - Blood sampling
    - Patient unstable/requiring resuscitation
    - Blood product transfusion
    - Parenteral nutrition
    - Chemotherapy
    - Unknown/Not documented
    - Other (specify)
  - Assessment of PIVC site is documented in the patient chart in the last 24 hours: yes, no
  - Site labeled with date and time of catheter insertion: yes, no.
  - Site overdue for relocation: yes, no. If yes: description for absence of relocation in medical records (yes, no)
  - Use of PIVC: continuous, intermittent

- Flush solution used to keep the PIVC open:
  - No flushing
  - 0.9% sodium chloride
  - Heparin/heparinized saline solution
  - Other (specify)
  - Not applicable (PIVC used continuously)
  - Unknown/Not documented

- IV medications and solutions infused using this PIVC within the last 24 hours:
  - Fluids without electrolytes
  - Antimicrobials
  - Analgesics
  - Sedation
  - Other (specify)
  - None
  - Unknown/Not documented

- PIVC gauge/size:
  - 14G (orange)
  - 16G (grey)
  - 18G (green)
  - 20G (pink)
  - 22G (blue)
  - 24G (yellow)
  - 26G (purple)
  - Steel needle
  - Not visible
  - Other (specify)

- PIVC and administration set (extension tubing) securement
  - Sutureless securement device
  - Sterile tape strips around PIVC
  - Non-sterile tape around PIVC
  - Non-sterile tape over PIVC dressing
  - Non-sterile tape around administration set
  - IV administration set securement device
  - Splint/bandage/tubular net
  - Site dressing only
  - Other (specify)

- IV connectors:
  - Extension tubing
  - Stopcock/3-way tap
  - Needleless connector directly attached to catheter hub
  - Cap attached to the end of the catheter
  - IV tubing directly connected to catheter
  - Other (specify)
  - None

- PIVC dressing type:
  - Tape only (type of tape: paper, plastic, soft cloth, silk, other (specify))

- Gauze and tape dressing
- IV FIX
- Transparent film dressing
- Transparent film dressing and tape
- Bordered film dressing
- No dressing
- Other (specify)

- Signs and symptoms at the PIVC site: yes, no. If yes:
  - Pain/tenderness on palpation
  - Redness > 1 cm from insertion site
  - Swelling > 1 cm from insertion site
  - Purulence
  - Itch/rash under dressing
  - Blistering/skin tears under dressing
  - Dried blood
  - Palpable hard vein cord beyond IV tip
  - Streak/red line along vein
  - Induration/hardness of tissues > 1 cm
  - Other (specify)

- Presence of any of the following clinical complications: phlebitis (grade 1-4; mechanical, chemical, infective), hematoma, ecchymosis, skin injury, local infection.

- Presence of any of the following mechanical complications: catheter dislodgement, occlusion, extravasation, infiltration (grade 1-4), leaking at the insertion site.

- Presence of any of the following quality issues: unstable PVIC, blood reflux, uncontrolled IV infusion rate, site dressing partially detached, site dressing totally detached (site exposed to environment), medical tape added to dressing edges, unclean dressing, discomfort at site with or without palpation, uncovered tubing access port, lack of visibility at the PIVC site.

3.5 Randomization and Blinding

No blinding will occur during the study. As this is an observational study of existing PIVC practice and related complications, randomization is not applicable.

3.6 Study Materials and Labeling

There are no study materials, except for the study-specific questionnaires..

3.7 Study Duration

The study is expected to be open at each participating site until a minimum of 100 PIVC sites are assessed, so that a minimum of 300 PIVCs are assessed at all three participating hospitals.

Since this is an observational, cross-sectional study, each patient's involvement in the study will have a duration of one day only.

3.8 Study Termination

3M or the Investigator has the right to discontinue the study at any time for medical and/or administrative reasons. As far as possible, this should occur after mutual consultation.

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

- Failure of the Investigator to comply with pertinent ICH and ANVISA Regulatory Guidelines.
- Insufficient adherence to protocol requirements.
- Failure of the Investigator to complete the study at an acceptable rate.
- Submission of knowingly false information from the Investigator to 3M.
- Termination of Ethics Committee approval

3.9 Investigational Material Accountability

Based on the study design and lack of intervention, no investigational material will be provided or used in this study. Only the study-specific questionnaires to document the required study information will be distributed to the investigators. The investigator must keep the completed investigational questionnaires in a secure storage area, accessible only to authorized individuals.

3.10 Protocol Modifications

3.10.1 Protocol Amendments

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

3M will forward any significant protocol amendments to each study site's PI, who is responsible for submitting them to the Ethics Committee for approval.

3.10.2 Protocol Deviations

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

If the study personnel fail to obtain the subject's informed consent prior to data collection, then this would be considered a protocol deviation and the local Ethics Committee should be notified.

Deviations that potentially affect data integrity or compromise the statistical analysis of the study require immediate communication to 3M. The Investigator must contact the 3M study monitor within 24 hours of occurrence. A Protocol Deviation Form must be completed by the Investigator and include the type of deviation and a description of the circumstances surrounding the deviation. A copy is sent to the 3M study monitor within 24 hours of identifying the occurrence. This kind of deviation should also be notified to the local Ethics Committee.

3.11 Computerized Systems

Computerized systems that will be used to create, modify, maintain, archive, retrieve or transmit data include, but may not be limited to:

- SAS

- Excel
- Word
- Microsoft Outlook

4. Subject Selection

The study population will include adult patients admitted to the wards of the participating acute care hospitals that will be audited in the study. To minimize subject selection bias, all subjects will be identified and invited to participate in the study consecutively, as the auditor screens the ward on the day of the audit.

To be included in the study and for their PIVC sites to be evaluated, each patient should meet all of the inclusion criteria and none of the exclusion criteria described in the sections below. Subjects should provide written informed consent prior to any study-specific observations and data collection.

4.1 Subject Inclusion Criteria

Subjects must fulfil **all** the following inclusion criteria at the time of the audit to be included:

- Male or female subject, aged 18 years or older at the time of the study's audit of the ward;
- Subject admitted into one of the wards audited at the study site;
- Subject available for observation at the time of the audit;
- Subject with at least one inserted PIVC;
- Subject that voluntarily signed and dated the informed consent form (ICF) prior to study entry.

4.2 Subject Exclusion Criteria

Subjects must **not meet any** of the following exclusion criteria at the time of the audit to be included:

- Subject under treatment at the study site's outpatient clinics;
- Subject admitted into a mental health ward, emergency ward or burn unit;
- Subject awaiting transfer to another facility.

4.3 Subject Informed Consent

The Investigator at each site must obtain a written informed consent of all subjects to participate in the study, before study-related procedures. Full and adequate information about the nature, purpose, possible risks and benefits of the study must be provided. Subjects must also be notified that they are free to discontinue their participation in the study at any time. The subjects should be given the opportunity to ask questions and allowed time to consider the information provided.

As delineated in ResolutionNo466 and PANDRH-GCPs , the ICF content should be briefly and clearly presented orally, and in writing, in a manner that is easy to understand, commensurate with the comprehension level of the research participants, and without coercion or unduly influencing a potential participant to enroll in the study. Specifically, the Investigator is to explain to each subject all elements of informed consent as specified in ANVISA Regulatory Guidelines.

After the explanation, the subject or representative will voluntarily sign and date the consent form if they wish to participate in the study. An original version of the consent form must be provided to the subject. Another original signed and dated version of the ICF must be

maintained in the Investigator study documentation file at all times. The process of consent and study participation, with date, must be documented in the patient record/chart.

4.3.1 Confidentiality of study/subject data

The Subject ICF will incorporate wording that complies with relevant data protection and privacy legislation. Pursuant to this wording, subjects will authorize the collection, use and disclosure of their personal data by the Investigator and by those persons who need that information for the purposes of the study.

The Subject ICF will explain that study data will be stored in a computer database, maintaining confidentiality in accordance with the local law for Data Protection. The subject should be informed that all data will be anonymized and grouped for analysis, making it impossible to identify unique patient data.

The Subject ICF will also explain that, for quality check purposes, a monitor of 3M or designee, will require direct access to the signed subject ICFs and to the source documents that are part of the hospital or practice records relevant to the study.

5. Assessment of Safety

5.1 Adverse Events Definitions

An adverse event is any undesirable clinical occurrence, whether it is considered to be device- or drug-related or not.

5.2 Anticipated Device-Related Adverse Events

This an observational, cross-sectional study that is not designed to identify or quantify a safety hazard relating to an authorized medicinal product or medical device. Nevertheless, there are anticipated device-related adverse events that may occur during this study and are related to the current practice of PIVC therapy at the study sites. According to IV professionals and IV-related literature, the anticipated device-related adverse events that may occur are:

1. Certain skin reactions, such as mild to moderate redness, blisters, itching, and/or minor skin denudations at the site of the adhesive which should dissipate within one to seven days after removal;
2. Loss of the PIVC from the insertion site;
3. Leaking of fluid or blood from PIVC insertion site;
4. Phlebitis and/or;
5. Infiltration of an infusate.

5.3 Unanticipated/Serious Device Related Adverse Events:

The following list of unanticipated and/or more serious device-related adverse events are unlikely to be identified during this study, unless the audit nurse reads of the event during the medical record review. Excluding the severe skin reactions, the nurse auditors will most likely not be aware of the following unanticipated and/or serious adverse events:

1. Any catheter-related phlebitis with a fever;
2. A catheter-related phlebitis or infiltration that extends hospitalization;
3. A catheter-related blood stream infection (PIV-CRBSI);
4. Severe skin stripping or skin reaction; or
5. Extravasation.

5.4 Recording and Reporting Adverse Events

PIVC-related adverse events can occur at any time during the conduct of the study and may be identified by the Investigator (or designee), auditor or patient. The auditor who observes a PIVC-related adverse event or is told of an adverse event by the patient is responsible for reporting the event to the nurse caring for the patient. The patient's nurse and/or physician will be responsible for treating the patient. The country's and/or hospital's formal adverse event (incident) reporting process will be used to document the adverse event.

If the PIVC-related adverse event is also a PIVC-related complication of interest for the study (Section 3.3), their presence will be documented by study personnel in the corresponding Individual PIVC Questionnaire. There is no requirement for any additional information on adverse events to be recorded in the eCRF. Further details on adverse events that are also complications of interest for the study will be processed in accordance with the abovementioned country's or hospital's formal adverse event (incident) reporting process.

6. Statistics

6.1 Study endpoints

6.1.1 Primary endpoint

- Proportion of PIVCs sites with at least one clinical or mechanical complication.

6.1.2 Secondary endpoints

- Proportion of PIVC sites with at least one clinical and one mechanical complication.
- Proportion of PIVC sites with at least one clinical complication and with each specific clinical complication.
- Proportion of PIVC sites with at least one mechanical complication and with each specific mechanical complication.
- Proportion of PIVC sites with at least one related quality issue and with each specific quality issue.
- Frequency distribution for the PIVC Standards of Practice.

6.1.3 Exploratory endpoints

Measures of association between PIVC-related complications and sociodemographic characteristics, as well as between PVIC-related complications and other baseline characteristics will be examined, if appropriate.

6.2 Statistical Methods

6.2.1 General aspects

For the purposes of the present study, the unit of analysis will be the individual PIVC sites and not the patients in which they are inserted.

Descriptive statistics will be obtained for numerical variables, including central tendency measures such as mean, median as well as the dispersion measures of standard deviation, min-max and inter-quartile range. Descriptive statistics for categorical variables will include frequencies' tabulation with counts and percentages. No imputation of missing values will be made. 95% confidence intervals will be used if applicable. The significance tests of association under exploratory analyses will be made at the 5% significance level.

Data will be presented for the overall study sample, as well by hospital and by hospital ward.

6.2.2 Primary endpoint analysis

The prevalence of PIVC-related complications among the PIVC sites audited at the participating acute care hospitals in Brazil will be determined as follows:

- Prevalence (%) = (Number of audited PIVC sites with at least one clinical or mechanical complication ÷ Number of audited PIVC sites) x 100

The definitions of clinical and mechanical complications are detailed in Section 3.3 and Appendix I.

6.2.3 Secondary endpoint analyses

- The prevalence of PIVC-related clinical and mechanical complications among the PIVC sites audited at the participating acute care hospitals in Brazil will be determined as follows:
  - → Prevalence (%) = (Number of audited PIVC sites with at least one clinical and one mechanical complication ÷ Number of audited PIVC sites) x 100

- The prevalence of PIVC-related clinical complications among the PIVC sites audited at the participating acute care hospitals in Brazil will be determined as follows:
  - → Prevalence (%) = (Number of audited PIVC sites with at least one clinical complication ÷ Number of audited PIVC sites) x 100
  - → Prevalence (%) = (Number of audited PIVC sites with each specific clinical complication ÷ Number of audited PIVC sites) x 100

- The prevalence of PIVC-related mechanical complications among the PIVC sites audited at the participating acute care hospitals in Brazil will be determined as follows:
  - → Prevalence (%) = (Number of audited PIVC sites with at least one mechanical complication ÷ Number of audited PIVC sites) x 100
  - → Prevalence (%) = (Number of audited PIVC sites with each specific mechanical complication ÷ Number of audited PIVC sites) x 100

- The prevalence of PIVC-related quality issues among the PIVC sites audited at the participating acute care hospitals in Brazil will be determined as follows:
  - → Prevalence (%) = (Number of audited PIVC sites with at least one quality issue÷ Number of audited PIVC sites) x 100
  - → Prevalence (%) = (Number of audited PIVC sites with each specific quality issue ÷ Number of audited PIVC sites) x 100

The definitions of clinical and mechanical complications, as well as of quality issues, are detailed in Section 3.3 and Appendix I.

PIVC Standards of Practice will be summarized using descriptive statistics.

6.2.4 Exploratory endpoint analyses

Exploratory analyses will be performed with the aim of identifying the subject- and PIVC characteristics associated with the occurrence of PIVC-related complications.

The association of qualitative variables with the occurrence of PIVC-related complications will be performed with the chi-squared test or with the Fisher's test, while the association of quantitative variables with the occurrence of PIVC-related complications will be performed with the student's t test or the Mann-Whitney test.

Generalized estimating equation (GEEs) models will be used to identify the most important patient characteristics associated with the multivariate binary occurrence of PIVC-related complications, with a Logit link function and considering the correlation structure assumed as exchangeable within patients. The Odds Ratios as well as 95% confidence intervals will be estimated. The significance level will be established at 5%.

6.3 Sample Size Justification

No formal sample size calculation has been performed. Based on expert knowledge, it is assumed that a minimum of 100 PIVCs audited per hospital (or a total of 300 PIVCs audited in the study) will provide an adequate estimate of the prevalence of PIVC-related complications. In case a site experiences difficulty in meeting the expected recruitment rate, other participating sites may be proposed to include an additional number of patients, until the total is achieved.

6.4 Procedures to Account for Missing, Unused, and Spurious Data

Investigation of spurious and/or missing data will be discussed in the final report. Imputation of missing data will not be performed. Non-use of data will be described and justified in the final report.

6.5 Deviations to Statistical Plan

Any deviation(s) from the original statistical plan should be described and justified in the in the final report, as appropriate.

7. Monitoring

3M, as sponsor of this study, is responsible for ensuring the proper conduct of the study regarding adherence to the protocol, as well as to the applicable legislation and regulation, and the validity of the data recorded on the eCRFs. Monitoring activities will be performed at the study sites by:

- Periodic on-site review
- Telephone communications
- Review of eCRFs and source documents (e.g. patient hospital records, clinical charts, doctor's notes, Informed Consent Form, etc.)

The Investigator will give the 3M and the CRO study monitor direct access to source documents that support data on the eCRFs and make available such records to authorized 3M personnel, Quality Assurance personnel, Ethics Committee, and regulatory personnel for inspection.

8. Quality Control and Quality Assurance

3M is responsible for implementing and maintaining quality assurance and quality control systems through written standard operating procedures (SOPs) to ensure that this study is conducted, and data are generated, documented and reported in compliance with the protocol, GCP and regulations cited in Section 1.5 of this protocol. Study monitoring will be carried out to accomplish this.

9. Ethics

The study will be conducted in compliance with the protocol, the foundational principles on the Declaration of Helsinki, ICH's GCP and all applicable regulatory requirements.

This research project was prepared in accordance with Resolution No. 466 of December 12, 2012 of the National Health Council, which establishes the ethical standards for research involving human beings. The study will start only after approval of the protocol and of the ICF by the Ethics Committee and after the Research Agreement has been established with the site.

3M must receive a copy of the Ethics Committee approval letter prior to study initiation.

10. Data Handling and Record Keeping

10.1 Study Personnel

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

10.2 Pre-Study Documentation Requirements

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

- Signed protocol including any amendments in place prior to study initiation;
- Curriculum vitae for all study staff;
- Ethics Committee study approval letter;
- Ethics Committee approved consent form;
- Ethics Committee name, location and chairperson;
- Signed research agreement.

10.3 Completion and Return of Case Report Forms (CRFs)

The Investigator will review all eCRFs for completeness and accuracy. If a correction is required, a single line must be drawn through the error. The person making the correction will initial, date, and provide a reason for the error (if not self-evident).

The Investigator must attest to the quality, accuracy and completeness of all eCRFs in a timely fashion. The monitor will review the eCRFs to assure accuracy and completeness. Any data queries prepared after the eCRFs have been completed must be answered promptly.

10.4 Records, Reports and Retention Requirements

The Investigator will maintain study records for a minimum of 5 years following completion of the study. Records that must be maintained by the Investigator include, but are not restricted to:

- Signed study protocol, amendments and protocol deviations;
- Ethics Committee approval of protocol, ICF and amendments to any of these documents;

- Applications to the Ethics Committee;
- Signed ICFs;
- Study-specific questionnaires;
- Correspondence relating to the study;
- Sponsor Final Report.

11. References

1. PR Newswire. Global Peripheral I.V. catheter market 2014-2018.
2. Rickard CM, Webster J, Allis MC. Routine versus clinically indicated replacement of peripheral intravenous catheters: a randomized controlled equivalence trial. Lancet. 2012; 380 (9847): 1066-1074
3. Webster J, Clarke S, Peterson D, et al. Routine care of peripheral intravenous catheters versus clinically indicated replacement randomized controlled trial. BMJ. 2008; 337: 1-6.
4. Bausone-Gazda D, Lefavier CA, Walters SA. A randomized controlled trial to compare the complications of 2 peripheral intravenous stabilization systems. J Infus Nurs. 2010; 33 (6): 371-384.
5. Martinez JA, Piazuelo M, Almela M, et al. Evaluation of add-on devices for the prevention of phlebitis and other complications associated with the use of peripheral catheters in hospitalized adults: a randomized controlled study. J Hosp Infect. 2009; 73 (2): 135-142.
6. Maki DG. Improving the safety of peripheral intravenous catheters. BMJ 2008; 337: 122-23.
7. Wallis MC, McGrail MR, Webster J et al. Risk factors for PIV catheter failure: a multivariate analysis from a randomized control trial. Infect Control Hosp Epidemiol 2014; 35 (1): 63-68.
8. Alexandrou E, Ray-Barruel G, et al. International Prevalence of the Use of Peripheral Intravenous Catheters. Journal of Hospital Medicine 2015; 00(00): 1-4.
9. Gorski L, Hadaway L, et al. Infusion Therapy Standards of Practice. Journal of Infusion Nursing 2016; 39 (1S).
10. Mattox, E. Complications of Peripheral Venous Access Devices: Prevention, Detection, and Recovery Strategies CriticalCareNurse 2017; 37(2): e1-e14.
11. Helm, R et al. Accepted but Unacceptable: Peripheral IV Catheter Failure. Journal of Infusion Nursing, 38(3), 189-203.
12. Marsh, N et al. Securement methods for peripheral venous catheters to prevent failure: a randomized controlled pilot study. JVasc Access 2015; 00(00): 1-8.

12. Appendices

12.1 Appendix I– Definition of PIVC-related complications

Table A – Definition of clinical PIVC-related complications

Complication	Definition
Phlebitis	Presence of pain, tenderness, warmth, erythema or streak formation at or near the PIV insertion site due to movement, chemical irritant and/or bacteria. Thus, according to etiology, phlebitis may be classified as: • Mechanical: If the catheter is dislodged or not secure (i.e., moves) • Chemical: If the patient is receiving, KCl, IV fluids or antibiotics that tend to cause phlebitis • Infective: if local infection is also present The degree of phlebitis is rated using a scale ranging from 1 to 4[a]: • Grade 1: Erythema at access site with or without pain. • Grade 2: Pain at access site with erythema and/or edema. • Grade 3: Pain at access site with erythema, streak formation, and/or palpable venous cord. • Grade 4: Pain at access site with erythema, streak formation, palpable venous cord >1 inch in length, and/or purulent drainage.
Hematoma	A localized swelling that is filled with blood caused by a break in the wall of a blood vessel.
Ecchymosis	Similar to a hematoma. A subcutaneous spot of bleeding (from extravasation of blood) with diameter larger than 1 centimeter.
Skin injury	Superficial damage to the skin as seen by redness, tears, or erosion of the skin, or development of blisters in an area exposed to medical adhesive and lasting for 30 minutes or more.
Local infection	Redness and/or induration within 2 cm of exit site with or without purulent drainage.

a. From: Alexander M. Corrigan A. Infusion Nurses Society: Infusion nursing an evidence-based approach. St. Louis, Mo.: Saunders-Elsevier; 2010.

Table B – Definition of mechanical PIVC-related complications

Complication	Definition
Catheter dislodgement	Movement of the PIV catheter out of the insertion site to the point it cannot be safely used, excluding infiltration.
Occlusion	Stopping or slowing of I.V. fluid flowing from the I.V. bag into the bloodstream. Signs: one is unable to easily flush fluid into the catheter without resistance. Causes: blood clotting in the catheter, kinking of the catheter or tubing, an admixture of medications/fluids or a venous thrombosis.
Extravasation	Accidental infiltration of a vesicant or chemotherapeutic drug into the tissues surrounding the IV site resulting in edema and/or tissue necrosis.
Infiltration	When a solution or medication enters the surrounding tissues due to catheter dislodgement or vein ruptures. Recognized by increasing edema at or near the venipuncture site. The degree of infiltration is rated using a scale ranging from 1 to 4: • Grade 1: Skin blanched; edema <1 inch in any direction; cool to touch; with or without pain. • Grade 2: Skin blanched; edema 1-6 inches in any direction; cool to touch; with or without pain • Grade 3: Skin blanched, translucent; gross edema>6 inches in any direction; cool to touch; mild-moderate pain; possible numbness. • Grade 4: Skin blanched, translucent; skin tight, leaking; skin discolored, bruised, swollen; gross edema>6 inches in any direction; deep pitting tissue edema: circulatory impairment; moderate-severe pain; infiltration of any amount of blood product, irritant, or vesicant.
Leaking at the infusion site	IV fluid found under the dressing that is exiting the catheter insertion site.

a. From: Alexander M. Corrigan A. Infusion Nurses Society: Infusion nursing an evidence-based approach. St. Louis, Mo.: Saunders-Elsevier; 2010.

Table C – Definition of PIVC-related Quality issues

Issue	Definition
Unstable PIVC	Catheter moves when touched or when patient moves yet is still functioning.
Blood reflux	Blood observed in the tubing, not associated with a recent blood infusion.
Uncontrolled IV infusion rate	Infusion rate controlled by only a roller clamp or by gravity.
Site dressing partially detached	Dressing is lifted off skin, but insertion site not exposed to environment (25% or greater)
Site dressing totally detached	Dressing is lifted off skin and insertion site exposed to environment
Medical tape added to dressing edges	Tape added to the edges of the insertion site cover or dressing to prevent the dressing from lifting up off the skin either due to the presence of edge lift or to prevent lift from occurring.
Unclean dressing	Stains or dirt observed on the dressing due to blood, food, secretions and/or other outside contaminants
Discomfort at the site with or without palpation	When subject states that the catheter is painful or uncomfortable, if asked, OR when subject complains of pain when the catheter insertion site is touched (palpated).
Uncovered tubing access port	An access port that is open to the environment without a cover or cap
Lack of visibility	When the auditor cannot see the catheter insertion site due to (1) the opacity of the dressing, e.g. tape dressing or (2) tape, gauze pad or patch used under a film dressing.