RESEARCH PROTOCOL INVOLVING HUMAN SUBJECTS

NON - INTERVENTIONNAL

Eva Study

STUDY OF SPEEDICATH CATHETER SELECTION CRITERIA AT START OF SELF-CATHETERISATION

ID-RCB (Registration number of the study) no.: 2021-A00579-32

SPONSOR	COORDINATING INVESTIGATOR
COLOPLAST 6 rue de Rome 93 561 Rosny sous Bois cedex - France Tel.: 01 56 63 17 81 Email: frsme@coloplast.com	Prof. Gerard Amarenco Department of Neuro-Urology, Hôpital Tenon [Tenon Hospital], Paris 4 Rue de la Chine, 75020 Paris, France Tel.: 01 56 01 75 00/01 56 01 76 13 Email: gerard.amarenco@aphp.fr

Final version 3.0 03/09/2021

LIST OF ABBREVIATIONS

ANSM: Agence Nationale de Sécurité du Médicament [French National Agency for Medicines and Health Products Safety]
ISC: Intermittent Self-Catheterisation
GCP: Good Clinical Practices
EC: Ethics Committee
CNIL: Commission Nationale Informatique et Libertés [French Data Protection Authority]
CPP: Comité de Protection des Personnes [Ethics Committee]
CRF or eCRF: electronic case report form
CRO: Contract Research Organization
CSP: Code de la Santé Publique [French Public Health Code]
MD: Medical Device
AE: Adverse Event
SAE: Serious Adverse Event
USAE: Unexpected Serious Adverse Event
GENULF: Groupe d'Études de Neuro-Urologie de Langue Française [French Neuro-Urology Study Group]
I-CAS: Intermittent Catheterisation Adherence Scale
I-CAT: Intermittent Catheterisation Acceptance Test
IC-Di-Q: Intermittent Catheterisation Difficulty Questionnaire
SC: SpeediCath

TABLE OF CONTENTS

1 SYNOPSIS

Title	STUDY OF SPEEDICATH CATHETER SELECTION CRITERIA AT THE START OF SELF-CATHETERISATION
Short title	Eva
Sponsor	COLOPLAST
Coordinator	Prof. Gerard Amarenco
Trial type	Multicentre observational study
Objectives	**Primary objective:** Specify the final choice criteria for the type of SpeediCath (SC) catheter that provides patient satisfaction determined by self-questionnaire at V3 **Secondary objectives:** - Document the reasons for the patient's initial choice of the SC catheter: determined by self-questionnaire at V1 - Determine the patient's adherence to Intermittent Self-Catheterisation (ISC) at the end of follow-up and his/her development over the first six months: measured by I-CAS at V2 and V3 - Document patient satisfaction with the catheter: measured on a five point scale at V2 and V3 - Document challenges during the first six months of the ISC: measured by the IC-Di-Q at V2 and V3 - Determine the variables associated with the catheter selection and adherence to the ISC.
Eligibility criteria	**Inclusion criteria** • Female or male aged eighteen years or older • Subject informed of the study and who decided to participate in it (non-opposition) • Subject affiliated with a social security scheme or beneficiary • Subject with neurogenic or non-neurogenic bladder issues, justifying the implementation of ISC to empty the bladder • Subject who received his/her initial ISC training at the time of inclusion • Subject for whom the expected ISC duration is at least six months • Subject for whom at least two types of SC catheters have been introduced and who has chosen to use the catheters from the SpeediCath range as the first catheter for self-catheterisation • Subject able to independently conduct ISC • Subject for whom the healthcare professional has recommended to conduct ISC at least four times per day

	<u>Exclusion criteria</u> • Vulnerable subject with regard to the current regulation • Pregnant, parturient or breast-feeding woman; • Subject deprived of freedom by judicial, medical or administrative decision; • Under age subject; • Subject legally protected or unable to express consent • Subject not affiliated with or not a beneficiary of a social security scheme; • Subject falling into several categories above; • Subject who refused to participate in the study • Subject participating in an interventional clinical study • Subject who, according to the investigator, has cognitive problems that prevent him/her from completing a questionnaire or for whom the assessment may be a problem.
Implementation of the study	The study will be offered to all adult subjects with neurogenic or non-neurogenic bladder issues, newly initiated at ISC and users of catheters from the SpeediCath range. The study will be conducted in three visits (inclusion visit, visit between 3 and 12 weeks, visit at 6 months) during which investigators will collect data specific to the self-catheterisation methods and to the use of catheters from the SpeediCath range, as well as a set of patient questionnaires. In the case of a catheter change during follow-up, the model and brand of the new catheter will be documented and the participant will continue the study.
Number of patients needed	**250 patients**
Study duration	Duration of inclusion period: 6 months Total study duration: approximately 12 months
Statistical analysis	A statistical analysis plan will be written after approval of the protocol. This document will have a reference value for the statistical analyses.

2 STUDY FLOWCHART

V1 - Screening Visit – Inclusion D0		
	Investigator	Patient information
		Inclusion and non-inclusion criteria
		Socio-demographic data
		Clinical data and scores
		Acceptance of the ISC (I-CAT)
		Concomitant bladder treatments
		Method for choosing the catheter and the patient's criteria for choosing the catheter
		Education conditions and ISC methods
		Adverse events
V2 - Follow-up visit - 3 to 12 weeks		
	Investigator	Clinical data
		Continuation of ISC
		Continued use of chosen catheter
		Concomitant bladder treatments
		Adverse events
	Patient	Daily frequency of the ISC
		Overall impression with the ISC
		Satisfaction with the catheter (on a five point scale)
		Challenges during the ISC (IC-Di-Q)
		ISC adherence (I-CAS)
V3 - End of study visit – around 6 months		
	Investigator	Clinical data
		Continuation of ISC
		Continued use of chosen catheter.
		Concomitant bladder treatments
		Adverse events
	Patient	Daily frequency of the ISC
		Overall impression with the ISC
		Satisfaction with the catheter (on a five point scale)
		Patient's final choice criteria for the catheter
		Challenges during the ISC (IC-Di-Q)
		ISC adherence (I-CAS)

3 STUDY RATIONALE

Urinary self-catheterisation involves emptying your bladder on your own by inserting a catheter into the urethra. This is the standard method in the case of dysfunctions of the bladder clean-out phase, particularly in the case of complete urinary retention or complete or incomplete bladder clean-outwith subvesical obstruction.[1] Neurological conditions such as spinal cord injuries, multiple sclerosis, multiple system atrophy, peripheral neuropathies, or Parkinson's disease and stroke can cause bladder disturbances. These disturbances can also result from pelvic denervations that are consequences of extended pelvic surgeries or radiation therapy intended for the treatment of gynaecological, urological or digestive cancers.[2]

The goal of ISC implementation is to reduce the morbidity related to vesico-sphincter dysfunction and improve the quality of life of patients by making them more independent.[2]

It involves for the patient a rigorous learning phase and an acceptance phase of this new micturition mode.[2]

When intermittent self-catheterisation (ISC) is indicated, training is provided to the patient in order to enable him/her to manage the catheterisation on a daily basis. The objectives of this study are to understand, achieve, monitor and adapt self-care. This training, primarily provided by the nursing staff and/or a specialist doctor, is usually ensured during an admission to hospital.[2] After returning home, the patient continues to be monitored by the specialist doctor and the nursing team to assess the mastery of the technique (possibly review the procedure and ensure the suitability of the catheter), patient adaptation to ISC practice, his/her compliance with the associated rules (frequency and regularity of catheterisations, urine volume) and any complications. A first visit is usually performed between three and twelve weeks, then a second visit after six months of use.

But this patient therapeutic education (PTE), even performed by experienced and specifically trained staff, may not be sufficient for the patient's immediate acceptance and his/her adherence to self-catheterisation in the medium or long term.[2]

It is indeed appropriate for the patient to be a participant in his/her choice, at least for the equipment, since it is usually up to the doctor to decide on self-catheterisation and that the benefits of self-catheterisation outweigh the constraints. The patient should therefore be guided and involved in the choice of his/her catheter during this learning phase, ensuring better compliance and future adherence to the treatment.[2]

The interest of this study is therefore to better understand the patient's true motivations in choosing the catheter. This will likely allow for improvements in the future, either the equipment itself or certain PTE sequences, with a focus on problematic points or questions in terms of the choice of the catheter offered to the patient by the healthcare staff. The determinants of the patient's choice are all the more important as there are a very large number of catheters on the market.

That is how Coloplast offers a range of SpeediCath ® (SC) self-lubricated ready-to-use hydrophilic catheters. This range is designed to cover different patient needs, providing catheters with different lengths, flexibility, shapes and ergonomics. There are three types of catheters adapted to women (SC Standard®, SC Compact® and SC Compact Set, SC Compact Eve®), and three types of catheters adapted to men (SC Standard®, SC Compact® and SC Compact Set, SC Flex®).

With regard to technical specificities, a systematic review of the literature concluded that hydrophilic catheters (with a lubricant attached to the catheter) provided a benefit, in terms of safety and quality

of life, particularly in patients with spinal cord injuries.[2,3,] SC® catheters significantly reduce trauma to the urinary tract by reducing friction.[4,5] Another study also showed that the implementation of SpeediCath catheters was significantly faster, convenient and discrete, compared to a non-ready-to-use hydrophilic catheter (need to activate the lubricant).[5] The superiority of SpeediCath Compact Male and Female catheters in terms of quality of life compared to reference catheters was demonstrated in a randomised study using the validated specific ISC-Q questionnaire and was retained and valued by CNEDiMTS.[6,7]

To date, there is no objective data to help in the choice of the type of catheter to offer to the patient based on his/her needs. Although it is now known that the quality of life of patients practising ISC is dependent on multiple factors[2], there is little data on factors that facilitate or hinder adherence to ISC during the first six months, post-initiation to ISC.[8] The exploratory multicentre prospective observational study we want to conduct aims to determine which criteria are the patient's choice in terms of SC catheters. This information would allow in the future to be able to implement personalised advice with each patient, with the aim of offering them the SC catheter that best suits his/her needs. The study population will consist of adults with neurogenic or non-neurogenic bladder issues justifying the implementation of ISC, with ISC education occurring at the time of inclusion. Patients should be independent in the practice of ISC, and the minimum expected duration of follow-up should be greater than or equal to six months. Only patients who choose to use catheters from the SpeediCath range will be included in the study.

Many criteria will be collected to allow for a thorough analysis of the methods for choosing the type of SC catheter. This collection involves the use of patient self-questionnaires. These questionnaires will be collected during the patient's usual follow-up, including a visit at the time of ISC education, a follow-up visit around three to twelve weeks (depending on the investigator site practices) and a second follow-up visit around six months.

- ✓ ISC acceptance will be measured by the "Intermittent Catheterisation Acceptance Test" (I-CAT) questionnaire. This is a patient questionnaire developed by the French Language Neuro-Urology Study Group (GENULF) and validated in French in 2016 in a multicentre prospective study conducted in 201 neurological and non-neurological patients.[9] The I-CAT helps to better assess and understand the psychological barriers that patients face in relation to ISC. The questionnaire consists of fourteen questions, with a minimum score of 0 for perfect acceptance, and the maximum score of 56 characterises the worst possible acceptance.

- ✓ The difficulties experienced by patients during the ISC will be measured by the Intermittent Catheterisation Difficulty Questionnaire IC-Di-Q. This is a patient questionnaire validated in French,[10] and aims to assess the difficulties encountered during the performance of the ISC. It explores in thirteen questions many factors such as pain, blockage, bleeding, spasticity, urethral sphincter spasm, in terms of frequency of occurrence and intensity. The purpose of this questionnaire is to identify the challenges faced by patients, and to follow up their progress after alternatives or solutions have been put in place (including adapting to the type of catheter).

- ✓ Patient adherence or compliance to the ISC will be measured by the Intermittent Catheterisation Adherence Scale (I-CAS). This is a patient questionnaire validated in French[11]consisting of eight questions, seven of which have a binary answer (yes/no) and one has five proposed responses. The score ranges from 0 for strong ISC adhesion to 8 for very low adhesion.

- ✓ A study-specific self-questionnaire was also created with the support of the scientific council to determine the reasons for the patient's choice of the catheter. This questionnaire includes the patient's independent criteria (e.g. nurse's advice) and patient-specific criteria (e.g. ease of use, discretion).

4 STUDY OBJECTIVES

The purpose of this exploratory study is to determine the major criteria in the choice of catheter by patients.

The results will allow for personalised counselling to be put in place for each patient, in order to offer him/her as a first-line treatment the catheter that is the most appropriate for his/her profile, with the goal of facilitating ISC learning and improving ISC adherence and acceptance.

4.1 Primary objective

The primary objective of this study is to specify the final criteria for choosing the SC catheter that provides patient satisfaction, as determined by self-questionnaire at V3.

4.2 Secondary objectives

The secondary objectives are as follows:

- Document the criteria for the patient's initial choice of the SC catheter: determined by self-questionnaire at V1
- Document patient satisfaction with the SC catheter: measured on a five point scale at V2 and V3
- Document the challenges encountered during the first six months of the ISC: measured by the IC-Di-Q at V2 and V3
- Determine patient adherence to the ISC over the first six months: measured by I-CAS at V2 and V3.
- Determine the variables associated with the catheter selection and adherence to the ISC.

5 METHODOLOGY

This is a prospective, multicentre, descriptive, observational, cohort study of routine care.
This research does not involve any additional risk to current practice and minimal constraints related to the conducting of questionnaires. All care procedures will be performed and the products used in the usual way.

5.1 Study Devices

General information

SpeediCath® is a range of four types of urinary catheters, available as different products with different sizes and also marketed in sets (pre-connected to bags). These are class 1 sterile devices with CE marking intended to be introduced into the urethra to clean out the bladder. This range is developed and manufactured by Coloplast A/S, 3050 Humlebaek, Denmark.

Product	First year of marketing
SpeediCath standard®	2000
SpeediCath Compact® Female	2005
SpeediCath Compact® Male	2011
SpeediCath Compact Eve®	2015
SpeediCath Flex ®	2017

The products from the SpeediCath® range will be used according to the indication provided and described in the instructions for use. The patient will follow his/her healthcare professional's recommendations for the ISC methods.

Description

The SpeediCath® range is a range of ready-to-use, self-lubricating hydrophilic catheters designed to meet all patient needs. It includes products for men and others for women. The main difference lies in the length of the catheter, adapted to the male and female anatomies. The products used in this study are the following:

- SpeediCath Standard is a standard 40 cm catheter for men and 20 cm for women. It also exists in 30 cm for adolescents.
- SpeediCath Compact is a catheter that helps improve convenience and discretion. It can be done by no-touch insertion of the catheter and is available for both men and women.
- SpeediCath Compact Eve is a female catheter only. It has a triangular shape that makes it easy to handle.
- SpeediCath Flex is a flexible catheter with a sealable sheath and multi-directional olive-shaped tip for easy insertion: it only exists for men.

SpeediCath Compact catheters also come in a set (already connected to a bag).

Handling

All subjects will be trained by the healthcare team to use the products according to current recommendations.

5.2 Duration of patient follow-up

The follow-up of participants in this study will be six months after ISC implementation and learning.

5.3 Planned total study duration

The total expected duration of the study is twelve months, with an inclusion period of six months and a follow-up period of six months.

5.4 Managing potential bias

5.4.1 Blinding

This is an open-label study of the management of ISC, therefore blinding is not applicable.

5.4.2 Bias

Not applicable

6 STUDY POPULATION

6.1 Participants

The study population will consist of adults with neurogenic and non-neurogenic bladder issues, newly initiated at ISC, and users of catheters from the SpeediCath range.

6.2 Eligibility criteria

6.2.1 Inclusion criteria

- Female or male aged eighteen years or older
- Subject informed of the study and who decided to participate in it (non-opposition)
- Subject affiliated with a social security scheme or beneficiary
- Subject with neurogenic or non-neurogenic bladder issues, justifying the implementation of intermittent self-catheterisation (ISC) to clean out the bladder
- Subject who received his/her initial ISC training at the time of inclusion
- Subject for whom the expected ISC duration is at least six months
- Subject for whom at least two types of SC catheters have been introduced and who has chosen to use the catheters from the SpeediCath range as the first catheter for self-catheterisation
- Subject able to independently conduct ISC
- Subject for whom the healthcare professional has recommended to conduct ISC at least four times per day

6.2.2 Exclusion criteria

- ✓ Vulnerable subject with regard to the current regulation
  - Pregnant, parturient or breast-feeding woman;
  - Subject deprived of freedom by judicial, medical or administrative decision;
  - Under age subject;
  - Subject is legally protected or unable to express his/her consent;
  - Subject not affiliated with or not a beneficiary of a social security scheme;
  - Subject falling into several categories above;
- ✓ Subject who refused to participate in the study
- ✓ Subject participating in an interventional clinical study
- ✓ Subject who, according to the investigator, has cognitive problems that prevent him/her from completing a questionnaire or for whom the assessment may be a problem.

6.3 Investigators

The investigators participating in this study will primarily be urologists or doctors in physical medicine and rehabilitation. Approximately fifty investigators are expected to recruit the 250 patients expected for the study. These sites will be located throughout France.

7 STUDY IMPLEMENTATION

7.1 Inclusion

The study is for people who are newly educated in ISC and who have chosen to use a catheter from the SpeediCath range after they have completed their self-catheterisation training. It will be conducted with approximately fifty investigator sites. To ensure good representativeness, the number of patients/sites will be limited to five.

In order to limit selection bias, investigators should propose, if possible, study participation to all eligible patients who are seen consecutively. Screened eligible patients will have been informed of the study and will have wanted to participate in it (non-opposition).

After verification of the screening criteria, informing the patient will be carried out. At the end of this step, and in the absence of patient opposition, a patient identification number will be assigned to him/her and will be used throughout the study.

7.2 Participation in the study

The subject's participation in the study does not involve any additional examinations compared to the usual management of a patient. The study will be offered to subjects until the threshold headcount is reached at each site or until the total headcount is reached.

Since the study is observational, patients are free to make the decision to change catheters during follow-up if the initially chosen catheter is not suitable for them. In this case, this change will be documented as well as the model and brand of the new catheter chosen and the patient will continue the study normally.

7.3 Withdrawal from the study

Enrolled patients who meet at least one of the following criteria will be withdrawn from the study:

- Participant opposed to continuing the study,
- Participant who stopped self-catheterisation.

8 COLLECTED DATA

Screening and inclusion visit

During this visit, the following data will be recorded in the case report form:

- Unique identifier number;
- Date of visit;
- Patient's socio-demographic data: gender, age, living alone or with someone, professional activity, level of education
- Patient's clinical data: pathology and degree of involvement, history (age of bladder issues, bladder clean out mode, urinary symptoms (USP score), concomitant bladder treatments), anorectal dysfunction (considering the impact of these disorders on vesico-sphincter balance)[2], accessibility of urinary meatus (manual dexterity, upper limb joint range of motion, mobility, limitation of lower limb abduction in women, vision disorders, obesity, overweight with significant apron belly, prolapse in women), [2]urethral sensitivity (normal/decreased/increased)

- Acceptance questionnaire for I-CAT ISC
- Choice of catheter: catheters presented by the nurse, catheters tried by the patient, SpeediCath (SC) catheter chosen by the patient as the first catheter for self-catheterisation and the criteria that presided over this choice
- ISC learning terms and conditions: location, duration, number of trainings in the procedure, prescription of home nursing representative
- Recommended frequency for ISC
- ISC alone or associated with spontaneous urination
- Possible adverse events
- Date of next visit

Follow-up visit at three to twelve weeks

- Date of visit;
- Patient's clinical data. Urinary symptoms (USP score). Concomitant bladder treatments
- Self-catheterisation: methods of use, continuation of self-catheterisation, information on stopping, if applicable
- Catheter chosen: continue self-catheterisation with the chosen catheter or catheter change, information on the catheter change, if applicable
- Patient questionnaire on catheter use and satisfaction (on a five point scale),
- IC-Di-Q
- I-CAS
- Possible adverse events
- Date of next visit

End-of-study visit at six months

- Date of visit;
- Patient's clinical data. Urinary symptoms (USP score). Concomitant bladder treatments
- Self-catheterisation: methods of use, continuation of self-catheterisation, information on stopping, if applicable
- Catheter chosen: continue self-catheterisation with the chosen catheter or catheter change, information on the catheter change, if applicable
- Patient questionnaire on catheter use and satisfaction (on a five point scale)
- IC-Di-Q
- I-CAS
- Possible adverse events

9 STATISTICS

9.1 Number of subjects needed

The primary objective of this study is to assess, with sufficient precision, the final criteria for choosing SpeediCath catheters.

In this context, the number of patients required depends on the desired precision for the frequencies observed of the choice criteria and the alpha risk. The table below shows that the precision obtained (95% confidence interval) for the percentages observed between 5% and 50% (or 95%-50% for the additional percentage) with 250 patients will be from ± 2.75% to 6.25% (± 2.75% for the percentages close to 95% or 5% and ± 6.25% for percentages close to 50%).

Number of patients required according to the desired precision (95% confidence interval) for an observed percentage (normal approximation).

Precision	Percent observed									
	5% / 95%	10% / 90%	15% / 85%	20% / 80%	25% / 75%	30% / 70%	35% / 65%	40% / 60%	45% / 55%	50% / 50%
± 2.5%	292	553	784	983	1152	1291	1398	1475	1521	1537
± 2.75%	241	457	648	813	952	1067	1156	1219	1257	1270
± 3.0%	203	384	544	683	800	896	971	1024	1056	1067
± 3.75%	130	246	348	437	512	574	621	656	676	683
± 4.0%	114	216	306	384	450	504	546	576	594	600
± 4.5%	90	171	242	304	356	398	432	455	470	474
± 5.0%	73	138	196	246	288	323	350	369	380	384
± 5.5%	60	114	162	203	238	267	289	305	314	317
± 6.0%	51	96	136	171	200	224	243	256	264	267
± 6.25%	47	88	125	157	184	206	224	236	243	246
± 6.5%	43	82	116	145	170	191	207	218	225	227

In summary, 250 patients will be needed in this study to allow for an assessment with sufficient accuracy (± 2.75% to ± 6.25%) of the final choice criteria for SC catheters.

And if we do not recover the final choice criteria of 10% of the enrolled patients (patients lost to follow-up, withdrawal of consent during the study, etc.), we will nevertheless have a precision ranging from ± 3.0% to ± 6.5% of the observed percentages.

Number of investigator sites and maximum number of patients per site.

Depending on the recruitment capacity of the investigator sites and the expected duration of the recruitment period, four to five patients will be enrolled per site with a maximum of twelve patients per investigator. As a result, a total of fifty active investigator sites will achieve the target of the 250 expected patients.

At the start of the study, forty investigator sites will be set up. If necessary, ten additional sites will then be added. Investigator sites will be selected to ensure representativeness in the treated patient population.

9.2 Statistical analysis

The analyses will be performed using the SAS V9.4 software (or earlier version), on a frozen database, after review of data allowing to identify protocol deviations and their potential impact on the analysis criteria. Protocol deviations will be classified as minor or major. Major deviations will lead to the exclusion of patients from the per protocol (PP) population. The distribution of patients in the analysis populations will be reviewed and approved by the sponsor before the database freeze.

The description of all the parameters will be based on the type of catheter and according to the gender of the patients. Quantitative parameters will be described using the following statistics: number of non-missing data, mean, standard deviation, median, first and third quartile, minimum and maximum. Qualitative parameters will be described using the headcounts and the percentages. These will be calculated from the number of non-missing observations. In all cases, the number of missing data will be specified.

Univariate analyses then multivariate analyses by logistic regressions will be performed to identify, among the data studied (patient choice criteria at V1, his/her final choice at V3, his/her adherence to ISC, his/her satisfaction with the catheter, his/her challenges during ISC, his/her clinical and socio-demographic characteristics, etc.), the predictive factors of the final choice of the SpeediCath catheter (Standard, Compact or Flex for male patients; Standard, Compact or Compact Eve for female patients).

The same will be done for adherence to ISC at V3 (with clinical and socio-demographic characteristics at V1, I-CAT score at V1, ICDQ score at V2, type of catheter chosen).

The other secondary endpoints will be described at the different time points and according to the catheter type.

Missing data at the time of analysis will not be replaced and will be considered as such.

A statistical analysis plan will be written after approval of the protocol. This document will have a reference value for the statistical analyses.

10 VIGILANCE

10.1 Definitions

10.1.1 Adverse event (ISO 14155:2020)

Any adverse clinical occurrence, unintentional illness or injury, or any adverse clinical sign (including abnormal laboratory results) in a subject, user or other individual, whether or not related to the investigational medical device. This definition includes events related to the investigational medical device. This definition also includes events related to the procedures involved.

10.1.2 Adverse reaction of a medical device (ISO 14155:2020)

Adverse event related to the use of the study medical device. This definition includes any adverse event resulting from insufficiencies or inadequacies in the instructions for use, roll-out, implantation, installation and functioning, or any malfunction of the study medical devices.

This definition includes any event resulting from a use error or from an intentional misuse of the investigational medical device.

10.1.3 Medical device incident (Article R5212-15 of the CSP)

The following incidents will also be reported:

- A harmful and unintended reaction that occurs when a medical device is used in accordance with its intended purpose;
- A harmful and unintended reaction resulting from the use of a medical device that does not follow the manufacturer's instructions;
- Any malfunction or alteration in the characteristics or performance of a medical device;
- Any incorrect indication, omission and insufficiency in the instructions for use, user manual or maintenance manual.

10.1.4 Serious adverse event (SAE) (ISO 14155:2020)

Adverse event leading to

- the death of the patient,
- a serious deterioration in the health of the subject that
    - caused a life-threatening illness or injury, or;
    - caused permanent infirmity of the body or bodily functions, or;
    - required an admission to hospital of the patient or extension of his/her hospital stay, or;
    - caused a medical or surgical procedure to prevent a life-threatening illness or injury to the subject or permanent infirmity of the body or bodily functions,

A planned admission to hospital due to a condition, without serious deterioration in health, is not considered a serious adverse event.

In the context of the study, any event deemed as medically significant by the investigator should be reported as a serious adverse event. The sponsor will treat the case according to the procedures applicable to adverse events.

10.1.5 Unanticipated serious adverse device effect USADE (ISO 14155:2020)

Serious adverse device effect whose nature, incidence, seriousness and consequences have not been identified in the current version of the safety reference document. An anticipated serious adverse device effect (anticipated SADE, ASADE) is an effect whose nature, incidence, seriousness, and consequences were identified in the risk analysis report.

10.1.6 Deficiency of the medical device

Any device deficiency related to its nature, quality, durability, reliability, safety or performance.

In this study, any decrease in efficacy or a safety parameter will be considered an AE. If the worsening is a subjective parameter, it should be correlated with at least one worsening of an objective parameter to be considered an AE.

Procedures such as surgery should not be considered an AE. However, the reason for which the procedure was conducted should be considered if it follows the definition of the AE as previously described.

10.2 Organisation and assessment

This protocol has no influence on medical prescription.
This study does not exempt the investigator healthcare professional from the immediate reporting to the ANSM of:

- Any incident or risk of serious incident that has led to or may lead to death or a serious deterioration in the health of a patient, user or third party involving a medical device must be reported (L.5212-2 and R.5212-14).

- Any recall of a medical device from the market, driven by a technical or medical reason, and which resulted in a systematic recall from the market by the manufacturer of the devices belonging to the same type.

Any incident or risk of serious incident concerning the device must be reported by the doctor to the ANSM's Monitoring Department, Receiving and Guidance Platform for Material Device Vigilance reporting.

The clinical course of each (serious) adverse event should be followed until the event (or its sequelae) is resolved or stabilised to an acceptable level for the healthcare professional or until the causal relationship to the device can be ruled out.

10.3 Role of the investigators

Any Incident or Serious Incident Risk that occurs during the course of the study must be reported to the ANSM's Monitoring Department, Receiving and Guidance Platform for Medical Device Vigilance reporting without delay, whether this involves:

- An unexpected serious adverse reaction (USAR);

- Serious adverse events likely to be related to the Medical Device implementation procedure;

- New safety events occurring during or after the end of the trial;

- A serious abnormal laboratory value.

Any Incident or Serious Incident Risk occurring during the course of the study must be reported, by the doctor, any harmful and unexpected reaction occurring:

- When used in a compliant manner that does not follow the manufacturer's instructions;

- Due to a malfunction or alteration in the characteristics or performance of a medical device or any inadequacy of labelling;

- Due to an omission or insufficiency of explanations in the instructions for use, user manual or maintenance manual.

However, any failure should not be reported when the safety features provided by the manufacturer have worked and dissatisfaction with the use of the medical device as long as it is not related to a safety defect.

Related or possibly related Adverse Events or Incidents or Serious Incident Risks must be collected and reported regardless of the time elapsed since the last study treatment dose, even if the study was closed.

Furthermore, since this protocol does not influence medical prescription, the healthcare professional participating in the study must report any Incident or Serious Incident Risk concerning the device, to the ANSM's Monitoring Department, Receiving and Guidance Platform for Medical Device Vigilance reporting, for which the accountability is deemed to be "yes" or "possible", as well as non-serious incidents for which the accountability is deemed to be "yes" or "possible" and unexpected.

Users or witnesses of an incident can also report to their local material device vigilance correspondent who is responsible for reporting to the ANSM.

All AEs occurring throughout the duration of the study planned in this protocol and observed by the investigator or reported by the participant will be reported in the CRF ("adverse event" form).

Any AE (serious or non-serious) must be documented in the "adverse event" tab of the CRF following the entry instructions.

The initial report should be as complete as possible by including dates of occurrence and completion, severity, seriousness, device or other device or medicinal product accountability, study procedures and actions taken.

Any information not available at the time of the event reporting should be documented in follow-up and an SAE will be followed up until it is considered as resolved or no longer progressing.

10.4 Role of the manufacturer

The manufacturer is responsible for the ongoing assessment of the medical device, which is the subject of the observational investigation. This includes the assessment of the causal relationship to the device, the seriousness and the expected or unexpected nature of the event.

The manufacturer will provide all relevant investigators with information that may affect the safety of the volunteers participating in this investigation, including in particular information on the nature and frequency of adverse reactions and events that may be related to the implementation procedure of the medical device.

10.5 Declaration of end of the research

The final study report will be written by the sponsor according to the reference plan and will be sent to the competent authority as well as to the CPP within a time limit of one year after the end of the

research, defined as being the last follow-up visit of the last subject enrolled. This will change to ninety days in the case of an early termination of the research.

11 ETHICAL AND REGULATORY CONSIDERATIONS

The sponsor and the investigators undertake that this research will be conducted in compliance with the law on the protection of persons participating in research involving human subjects, Jardé law (no. 2012-300) of 5 March 2012 modified by the law on public health policy (no. 2016-41) of 26 January 2016 and order no. 2016-800 of 16 June 2016, decree no. 2016-1536 of 16 November 2016, as well as in accordance with Good Clinical Practice (decision of 24 November 2006 and Standard ISO-14155: 2020) and with the Declaration of Helsinki.

Before starting the research, each investigator will provide the research sponsor's representative with a copy of his/her personal curriculum vitae, dated and signed.

11.1 Study conduct and Investigator's responsibilities

The healthcare professionals at each investigator site undertake to conduct the observational survey in accordance with the protocol that has been approved by the CPP. The investigator must not make any amendment to the protocol without the authorisation of the sponsor or its representative, and without the CPP giving a favourable opinion on the proposed amendments.

It is the responsibility of the principal investigator:

- to provide the sponsor's representative with his/her curriculum vitae as well as those of the co-investigators,
- to identify the members of his/her team participating in the trial and to define their responsibilities,
- to start recruiting patients after authorisation from the sponsor or its representative,
- to make every effort to include the required number of patients within the established recruitment period.

It is the responsibility of each investigator:

- to personally inform the patient and to ensure that there is no opposition before any trial-specific screening procedure,
- to regularly complete the case report forms (e-CRFs) for each patient enrolled in the trial,

All study-related documentation (protocol, information and non-opposition letters, case report forms, investigator file, etc.), as well as original documents (laboratory results, radiology results, consultation reports, reports for clinical examinations performed, etc.) must be kept in a secure location and considered as confidential material.

The archiving of data will be under the responsibility of the investigator and according to current legislation. The investigator will keep the data as well as a patient identification list for a minimum of fifteen years after the end of the study.

11.2 Committee for the Protection of Persons (CPP)

Before the start of the study, the protocol, all amendments, the information and non-opposition letter, any other information given to the patient, subject recruitment procedures, if applicable, the instructions for use, information on patient payments and compensation, if not mentioned in the information sheet, the up-to-date CV of the investigator and/or other documents proving his/her qualifications, and other documents required by the local ethics committee (EC) must be submitted. Written approval/favourable opinion must be obtained from the EC prior to the start of the study.

In accordance with Article L.1123-6 of the French Public Health Code, the research protocol must be submitted by the sponsor to a Committee for the Protection of Persons. The opinion of this committee is notified to the competent authority by the sponsor before the start of the research.

During the study, the sponsor or the CRO shall promptly report the following to the EC: updates of the instructions for use, unexpected SAEs for which a causal relationship cannot be ruled out, substantial amendments to the protocol, non-substantial amendments, protocol deviations and the means implemented to limit the immediate risks incurred by patients, any new information that may affect patient safety or the conduct of the study (including new risks/benefits in the case where it would impact patient follow-up), every year, the study status summaries, as well as any other documents required by the EC.

Substantial amendments cannot be implemented before approval/favourable opinion, unless they are necessary to eliminate risks for patients.

The sponsor must keep an accurate and complete record of all declarations made to the EC. The documents must be filed in the investigator file and copies must be sent to the sponsor or to the service provider.

11.3 CNIL

The data recorded during this research will be subject to computerised processing in accordance with the law no. 78-17 of 6 January 1978 relating to information technology, files, and civil liberties, modified by law 2018-493 of 20 June 2018.

This research is part of an undertaking of compliance with the “Reference methodology” (MR-003) of the CNIL pursuant to the provisions of Article 54 paragraph 5 of the law of 6 January 1978 as amended relating to information, files and civil liberties. The Coloplast company has signed an undertaking to comply with this “Reference methodology” as controller.

As part of the new European regulation 2016/679 on the General Data Protection Regulation (GDPR) of 16 April 2016 and its implementation on 25 May 2018, the sponsor and the investigators will ensure that they follow the rules and inform patients of their rights.

11.4 Sending of the agreement to the Council of the Board of Physicians

In application of Article L.4113-6 of the French Public Health Code, the sponsor’s representative will submit, for opinion prior to implementation, a standard agreement or the agreement established with the investigator to the National Council of the Board of Physicians, along with the required documents.

11.5 Informing of hospital representatives

The heads of the healthcare facilities will be informed of the conduct of the study in accordance with Article R. 1123-63 of the French Public Health Code. A hospital agreement will be carried out with each institution that requests it.

11.6 Protocol amendments

The sponsor and its service provider will be informed of any draft amendment of the protocol by the coordinating investigator.

The amendments will be classified as whether or not substantial.

After the start of the research, any substantial amendment to the research regarding the objectives of the study, its design, the population, the significant examinations or administrative aspects, and at the initiative of the sponsor must obtain, prior to its implementation, a favourable opinion from the ethics committee and an authorisation from the competent authority. In this case, if necessary, the committee will ensure that a new consent of the people participating in the research is properly collected.

In addition, any extension of the research (substantial modification of the design or populations enrolled) should be considered as new research.

11.7 Information of the patient and non-opposition

In order to obtain and document non-opposition, the investigator must comply with the current regulatory requirements.

Prior to any study-related activity, patients will be informed in a complete and fair manner, in understandable terms, of the objectives and their rights to refuse to participate in the study or the possibility to withdraw at any time.

The written information must mention the patient's right to request the rectification of the information and data collected about him/her, to require the correction of errors, to know who will be responsible for storing the data and who will have access to it.

In the case of opposition to the use of their sample for this research, patients should inform the doctor whose name and telephone number will be present on the information sheet.

The patient's non-opposition should be recorded in the patient's medical record.

11.8 Audits and inspections

The sponsor's quality manager (or qualified delegate) may organise audits of the study by verifying the procedures as well as the quality, authenticity and compliance with the source data of the information obtained. Direct access to the source documents is required to be able to conduct these audits.

Similarly, an administrative inspection, by an inspector delegated by the competent health authorities, is possible: acceptance of the protocol by the investigator also includes acceptance of the principle of this inspection of the study site.

11.9 Final research report

The final research report will be written by CLINACT, in collaboration with the sponsor, the coordinator, and the biostatistician, and any other relevant person. A report will be written according to the

competent authority's reference plan and will be sent to the competent authority as well as to the CPP within a time limit of one year after the end of the research, defined as being the last follow-up visit of the last subject enrolled. This will change to ninety days in the case of an early termination of the research.

12 RIGHT OF ACCESS TO DATA AND SOURCE DOCUMENTS

The healthcare professionals involved in this study will ensure that all the technical means used for the purposes of the study provide sufficient security in accordance with current rules for the exchange, sharing and storage of personal health data. COLOPLAST declares and warrants that it holds the mandatory approval for the hosting of personal health data under the conditions required by Article L.1111-8 of the CSP (from law no. 2002-303 of 4 March 2002 on patient rights and last amended by law 2016-41 of 26 January 2016 known as the modernisation of our healthcare system). The sponsor will ensure that the new regulation on the patient data for this study is followed. These rules are listed in the European GDPR regulation of 27 April 2016 and implemented since 25 May 2018.

12.1 Access to data

The sponsor will obtain agreement from all parties involved in the research in order to ensure direct access to all research locations, source data, source documents and reports for quality control and audit purposes.

The investigators will make available the individual documents and data strictly necessary for the follow-up, quality control and audit of research involving human subjects, to persons with access to these documents in accordance with current legal and regulatory provisions (Articles L.1121-3 and R.5121-13 of the CSP).

12.2 Source data

Any original document or item, including questionnaires proving the existence or accuracy of data or a recorded fact during the research, is defined as a source document.

12.3 Data privacy

In accordance with the current legal provisions, persons with direct access to the source data will take all necessary precautions to ensure the confidentiality of the information relating to investigational devices, research, participants volunteering for it and in particular with regard to their identity as well as the results obtained. These people, like the investigators themselves, are subject to professional secrecy.

13 QUALITY CONTROL AND ASSURANCE

13.1 Instructions for data collection

All information required by the protocol will be recorded in an electronic case report form and on the study questionnaires. An explanation will be provided for each piece of missing data. The data will be collected as they become available and recorded in a database. The database thus constituted does not make it possible to trace the patient's identity.

13.2 Data management

As part of this research, a processing of patient personal data will be implemented by CLINACT to allow for the analysis of the research results with regard to its objectives. Patient medical data will be sent to the research sponsor or to the people or companies acting on its behalf in France or abroad. These data will be identified by a code made up of the site code attached to the patient's order number. The patient's order number will be automatically assigned consecutively based on the inclusions. Only the healthcare professional will have a list of correspondence between this code and the patient contact information, kept by him/her in their office. Only this investigator may send the data to the study sponsor. These data may also, under conditions ensuring their confidentiality, be sent to French or foreign health authorities or to other entities of the study sponsor.

The sponsor will ensure that each person participating in the study has given his/her consent in writing for access to the individual data concerning him/her and strictly necessary for the quality control of the research.

13.3 Data management

CLINACT will be responsible for the data management activities of this study by implementing an ad hoc database, as well as an appropriate data validation and query resolution system. All data will be integrated into a database. Automatic and manual controls will be performed to ensure completeness, accuracy and consistency of the data. Adverse reactions will be coded according to the MedDRA dictionary. Concomitant treatments will be classified by ATC class according to the WHO-DRUG dictionary.

13.4 Audit and inspection

An audit may be conducted at any time by a competent authority or by persons authorised by the sponsor and independent of the research managers. Its objective is to ensure the quality of the research, the validity of its results and compliance with the law, operational procedures and current regulations.

The investigators agree to comply with the requirements of the sponsor and the competent authority for the purpose of a research audit or inspection.

The audit may apply at all stages of the research, from the development of the protocol to the publication of the results and to the filing of data used or produced as part of the research.

14 DATA PROCESSING AND STORAGE

Personal data protection and data circulation mode

Data management will be ensured by the specialist service company under contract with Coloplast. The data will be collected at the level of the participating doctors in an e-CRF previously developed and validated by the service company, hosted in France on an HDS server by a subcontractor of the service company.

The specialised service company will provide the study site with access to the e-CRF, which will have been fully validated in advance. Coloplast or the specialised service company in charge will train the study site staff on how the e-CRF works.

Access to the e-CRF will be via a unique login and password, assigned only after the e-CRF training has been completed with each potential user. The investigator team will enter the data defined by the protocol into the e-CRF using an on-site computer. To do this, the professional administrative data of the persons required to log into the e-CRF (CRAs, investigators, CRTs, etc.) will be used to create an account and manage their access in the application (e-CRF) by Coloplast or the specialised service company. These data will be limited to those listed in Article 3.2.3 of reference methodology MR-003.

A study-specific database will be created, tested and validated prior to the start of data entry. A data validation plan will be developed and will describe in detail the controls to be executed for each variable and thus ensure the quality of the data collected by the investigator. The obvious corrections must be validated by the investigator, who will be informed about the corrections on his/her site's data before the database freeze. The database will be frozen after a final quality control.

For the duration of the study, the original documents will be stored at the premises of the specialised service company under contract with Coloplast, with access to these documents being restricted to authorised persons only. They will then be prepared in archive boxes and sent to Coloplast for control and secure archiving.

Once the study is completed, the electronic data will be sent encrypted to Coloplast by the specialised service company, and the encryption key will be sent separately by another means of communication. Once Coloplast has confirmed the correct integrity of the electronic data, the specialised service company will destroy the active database on its server. Only an encrypted backup of this latest version of the database, held by the HDS host, to which the specialised service company can only have access upon written request, and which will be automatically destroyed by the HDS host thirty days after the active database is deleted by the service company.

Coloplast has an undertaking to comply with reference methodology MR-003 (declaration no. 2221608v0 of 22/03/2021) and the Eva study is in compliance with this reference methodology.

14.1 Data collection

All information required by the protocol must be reported in the eCRF under the responsibility of the principal investigator and an explanation must be provided for each piece of missing data.

14.2 General instructions

The eCRF is completed in English.

All data in the e-CRF will be consistent with the source documents, namely the patient's file or medical records.

Any discrepancies between the e-CRF data and the source document data will be documented directly in the database.

14.3 Data management

Data management will be conducted by CLINACT. A study-specific database will be created, tested and validated prior to the start of data entry. A data validation plan will be developed and will describe in detail the controls to be executed for each variable as well as the list of allowable obvious corrections.

The coding of medical terms and medicinal product names as well as the quality controls will be conducted by the data manager appointed by the sponsor in order to ensure the overall quality and consistency of the database.

Then the data will be controlled by the team responsible for data management while using the error messages from the validation programs.

At the end of the data management process, a data review meeting will be held in order to prepare the database freeze. After freezing the database, the data will be converted to SAS format for the conduct of statistical analyses.

Data processing, from data entry to the database freeze, will be performed according to the GCP (see ICH-E6, section 5).

The database will be frozen after a final quality control, then exported to the SAS statistical software (SAS Institute Inc., Cary, NC, USA) according to an automated and validated procedure.

15 TERMINATION OF THE RESEARCH

The primary contractor, sponsor, investigator or a competent regulatory authority may decide to terminate the study or part of the study at any time in accordance with current procedures.

If the study is terminated early or suspended, the investigator should promptly inform patients and ensure appropriate follow-up. In addition, the investigator, the sponsor or its representative must promptly inform the ethics committee and provide a detailed written explanation. The competent regulatory authorities shall be notified in accordance with current local regulations.

16 DEVIATIONS FROM THE PROTOCOL

No deviation from the protocol should occur. If deviations occur, the healthcare professional shall inform the principal investigator about it and the implications of the deviation shall be reviewed and discussed. Any deviation should be documented, including the reason and date, the corrective measures taken, as well as the consequences for the patient and/or the study. The documentation should be kept in the investigator binder and the sponsor's general file.

17 ARCHIVING

Patient observations should be kept in PDF format on a CD-ROM medium for the maximum period allowed by the hospital establishment, institution or private practice. The other source documents and the investigator binder must be retained for at least fifteen years or more in accordance with current local regulations.

The investigator must agree to archive the trial documentation in the archives after the end or the early termination of the trial, even if this is not specified. The investigator must not destroy the documents without prior authorisation from the sponsor or its representative.

The documents for research that fall within the scope of the law on research involving human subjects must be archived by all parties for a period of fifteen years after the end of the research. This indexed archiving will include:

- copies of the CPP's mandatory opinion and the ANSM information letter;
- the successive versions of the protocol (identified by the version no. and the version date);

- at the sponsor's site: the file and correspondence letters with the EC (including amendments);
- the correspondence letters with the sponsor;
- the corresponding enrolment list or record;
- For each enrolled patient, the eCRF will be signed electronically by the investigator and stored in PDF format,
- the audit trail;
- all appendices specific to the research;
- the final research report from the statistical analysis and from the quality control of the research (sent in duplicate to the sponsor);

The database that resulted in the statistical analysis must also be archived by the analysis manager (paper or digital format).

The sponsor will keep the trial documentation as long as the product/equipment is on the market or at least fifteen years after the end of the study, and in compliance with national regulations if they require a longer storage period.

18 DATA OWNERSHIP AND PUBLICATION RULES

The information obtained during the conduct of this trial is considered as confidential and is the property of the sponsor. It may be used by the latter for registration purposes and for the general development of the study product/equipment. All information provided by the sponsor or its representative in connection with this study is and remains the exclusive property of the sponsor and must be considered as confidential. No confidential information will be disclosed to third parties without the prior written consent of the sponsor or its representative and shall not be used outside the conduct of the study. The sponsor has the right to publish the full results of the trial. The targeted journal will be a national or international review of the highest possible impact factor based on study results.

In the case of disagreement regarding the content of any publication, the sponsor's opinion will be decisive.

In this multicentre trial, based on the collaboration of all sites, any publication of the results must recognise all sites.

19 BIBLIOGRAPHY

1. Gamé, X. *et al.* Intermittent catheterization: Clinical practice guidelines from Association Française d'Urologie (AFU), Groupe de Neuro-urologie de Langue Française (GENULF), Société Française de Médecine Physique et de Réadaptation (SOFMER) and Société Interdisciplinaire Francophone d'UroDynamique et de Pelvi-Périnéologie (SIFUD-PP). *Progrès en Urologie* **30**, 232–251 (2020).
2. Société française de Médecine physique et Réadaptation. Education Thérapeutique du Patient aux Autosondages (ETP-AS), guide méthodologique. (2019).
3. Chartier-Kastler, E. & Denys, P. Intermittent catheterization with hydrophilic catheters as a treatment of chronic neurogenic urinary retention. *Neurourol. Urodyn.* **30**, 21–31 (2011).
4. Stensballe, J., Looms, D., Nielsen, P. N. & Tvede, M. Hydrophilic-Coated Catheters for Intermittent Catheterisation Reduce Urethral Micro Trauma: A Prospective, Randomised, Participant-Blinded, Crossover Study of Three Different Types of Catheters. *European Urology* **48**, 978–983 (2005).
5. Pascoe, G. & Clovis, S. Evaluation of two coated catheters in intermittent self-catheterization. *British Journal of Nursing* **10**, 325–329 (2001).
6. Chartier-Kastler, E. *et al.* A Prospective, Randomized, Crossover, Multicenter Study Comparing Quality of Life Using Compact versus Standard Catheters for Intermittent Self-Catheterization. *Journal of Urology* **190**, 942–947 (2013).
7. CNEDiMTS. Rapport d'activité 2019 de la OMMISSION NATIONALE D'ÉVALUATION DES DISPOSITIFS MÉDICAUX ET DES TECHNOLOGIES DE SANTÉ. (2019).
8. Girotti, M. E., MacCornick, S., Perissé, H., Batezini, N. S. & Almeida, F. G. Determining the variables associated to clean intermittent self-catheterization adherence rate: one-year follow-up study. *Int. braz j urol.* **37**, 766–772 (2011).

9. Guinet-Lacoste, A. *et al.* Intermittent catheterization acceptance test (I-CAT): A tool to evaluate the global acceptance to practice clean intermittent self-catheterization. *Neurourology and Urodynamics* **36**, 1846–1854 (2017).

10. Guinet-Lacoste, A. Intermittent catheterization difficulty questionnaire (ICDQ): A new tool for the evaluation of patient difficulties with clean intermittent selfcatheterization. 5.

11. Guinet-Lacoste, A. *et al.* Intermittent Catheterization Adherence Scale (ICAS): A new tool for the evaluation of patient adherence with clean intermittent self-catheterization. *Neurourology and Urodynamics* **37**, 2753–2757 (2018).